The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 119, No. 13 — COPYRIGHT, 1942, BY AMERICAN MEDICAL ASSOCIATION — CHICAGO, ILLINOIS — JULY 25, 1942

MINIMIZING THE AFTER EFFECTS OF ACUTE POLIOMYELITIS

A RATIONALIZATION OF THE KENNY TREATMENT

CHAIRMAN'S ADDRESS

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NEW YORK

To pediatricians usually falls the care of poliomyelitis in its early stages. On them rests the responsibility of seeing that, at the time when they are most effective those measures are taken which are best able to save a maximum of function from the ravages of the disease. It is well that the Section on Pediatrics of the American Medical Association should devote a little time to surveying what it is that can best be done, and why.

At best, the treatment of poliomyelitis is as yet not satisfactory, because there is no specific serum, drug or chemical which will unquestionably cure or prevent the ravages of the disease. All treatment must be directed along the lines of symptomatic relief, helped of course by a study of the pathologic condition.

For years the outstanding pathologic feature has been considered to be paralysis due to loss of function of peripheral motor nerves, but as a result of the painstaking life work of the remarkable Australian nurse, Sister Kenny, and the recent studies of many medical research workers and clinicians, more and more persons are realizing that there are factors involved in muscle dysfunction in poliomyelitis other than loss of innervation and that much of the conception of the treatment of the disease held by most clinicians until recently must be changed. It is my purpose in this paper briefly to give the reasons for the necessity of this change and to summarize the present day treatment of choice of poliomyelitis.

CAUSES OF MUSCULAR DYSFUNCTION

The lesions in the spinal cord that occur early in poliomyelitis have been well known for some years. Those that affect the anterior horn cells can be classified under four headings: edema, perivascular infiltration, petechial hemorrhages and the additional direct effect of the virus itself on the motor neurons. The first three factors alter the nutrition of the nerve cells and presumably their function, but this effect is only temporary. The action of the virus on the neurons may be totally destructive, causing permanent loss of function, but on some of the anterior horn cells it may possibly cause only temporary damage, from which complete recovery is possible. Certainly at autopsy, on examination of a cross section of the spinal cord, it is not the rule to find complete destruction of all motor nerve cells in a given area; usually at least a few survive in any anterior horn. Just what proportion must be destroyed before there is a clinical evidence of loss of muscle function is not known. In patients dying of respiratory failure very early in an attack of poliomyelitis, examination of the spinal cord at autopsy frequently reveals a surprisingly extensive destruction of the anterior horn cells throughout the length of the cord, even though there may have been no gross clinical evidence of any weakness whatever in the arms or legs.

Studies on muscle physiology by Eccles and Sherrington and by Clark have indicated that each anterior horn cell in the spinal cord controls through its axon and collateral fibrils a group of muscle fibers which vary in number in the different muscles. The motor neuron with the muscle cells it supplies is called a motor unit, and there are many such in any given muscle. Those motor units whose neurons are killed in poliomyelitis are henceforth destroyed and cannot recover, but it is probably rare to have all destroyed, even in a small muscle. What happens to those that are not destroyed determines the end result of the injury to the muscle. The survivors in time may recover from the nonfatal influences on their respective neurons, but meanwhile, pending the subsidence of the temporary pathologic conditions in the spinal cord, these muscle fibers are subject to other harmful factors, particularly spasm.

Muscles in spasm are usually tender and painful and show a more or less tonic state of contraction of the muscle fibers, often apparently of the entire muscle. An additional form of spasm is the visible twitching, or fasciculation, which in the past has been considered of diagnostic significance as a probable precursor of paralysis. This consists in irregular contractions of the muscle fibers in groups of motor units and is presumably due usually to irritation of the anterior horn cells in the spinal column.

The causes of the more obvious spasm, that apparently involving an entire muscle or the greater part of it, are not clear. There are many theories at present, involving reflex action, irritation, circulation, inflammation and anoxia, which do not need to be gone into at this time. But whatever the cause, spasm certainly is constantly present in early poliomyelitis, being found in the muscles of the neck and the back, and in the hamstrings as well as in a variable number of other groups of muscles. It is found both in muscles most of whose motor neurons are definitely weakened or paralyzed and in those without any evidence of weakness.

Spasm causes dysfunction not only of the muscle that is in spasm but also of its antagonist, which may be overstretched and rendered noncontractile. For instance, spasm of the biceps affects the use not only of the biceps itself but also of the triceps. By oscillographic recordings of action currents, Schwartz and

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Read before the Section on Pediatrics at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1942.

Bouman of Rochester, N. Y., have recently proved that in the acute stage of poliomyelitis spasticity is found not only in the antagonists of weakened muscles but also in the weakened muscles themselves and furthermore in muscles elsewhere in the patient which show no clinical evidence of weakness.

Spasm is aggravated by pain and tenderness, by attempts at active motion, by forced immobilization as by casts and splints, also considerably by massage and by electrical stimulation. If untreated, muscle fibers in spasm may become hard and inelastic and may comprise the bulk of a muscle; eventually, some may show fatty replacement, others fibrous degeneration. Hipps also has described "stretch tears," or minute ruptures of bundles of muscle fibers due to the force of a slow, continued stretch. If spasm is allowed to persist, permanent contracture and further loss of function ensue.

As a result of these several factors, that is, the diminution of innervation, the presence of spasm, as already mentioned, and also because of muscle tenderness and pain, patients develop additional motor difficulties. There is a loss of ability to use muscles in proper relationship to one another and to the work to be done. This is called muscle incoordination by Sister Kenny and is illustrated by the substitution of an unsuitable or inefficient muscle for one that is weakened or in spasm. For example, when a patient has spasm of the intercostal muscles, he tries to breathe with his pectorals, with his sternocleidomastoids, and even with the platysma in the skin of the neck.

A second difficulty consists of a physiologic block preventing the proper transmission of a nerve impulse from the central nervous system to a contractable or nonparalyzed muscle, a condition known in the Kenny nomenclature as mental "alienation." Here there is no persisting organic injury to the motor units, but because of various factors the patient is unable to operate the motor neurons normally. Inhibition due to pain can cause "alienation," as can also spasm in an antagonistic muscle, or a temporary loss of function of the neurons due to pathologic factors in the spinal cord. Even after these influences have disappeared the "alienation" may persist, the patient having lost the power of accustomed control over the particular motor units involved.

Thus, to recapitulate, there are several causes of muscular dysfunction in poliomyelitis. First, a primary loss of innervation, with resulting actual paralysis; second, spasm of the surviving fibers in the involved muscle or in an antagonistic muscle; third, muscle incoordination; and, fourth, mental "alienation." Of these factors, only the first is irremediable and permanent. Destroyed motor units remain destroyed, and no newly formed or regenerated muscle cells will appear. Occasionally practically all the motor units in a particular muscle may be so involved, but much more commonly only a fraction of the motor units in any given muscle are killed. The rest are subject to spasm, incoordination and "alienation" and, unless these factors are counteracted, spasm overcome and the continued misuse of surviving muscles and parts of muscles prevented, otherwise viable motor units may eventually die, and contractures and further crippling may be produced.

No treatment will help dead motor units, but the Kenny treatment will rescue still living units from the effects of spasm, muscle incoordination and mental "alienation." It is believed that motor units which survive can develop a compensatory hypertrophy even to the extent of compensating for the killed units, so that there may be no apparent loss of function in a muscle that had seemed to be seriously involved. Therefore, I for one am convinced that the treatment of an acute case of poliomyelitis must include consideration of this pathologic conception of the causes of muscle dysfunction.

APPLICATION OF KENNY TREATMENT

We pediatricians would do well to put the Kenny technics in their proper place in the whole detailed care of early poliomyelitis. When a new patient comes to our attention there are four general groups of manifestations to the management of which should be devoted our most earnest endeavors. These are (1) toxicity, (2) spasm and its sequelae, muscle incoordination and mental "alienation," (3) certain difficulties such as of swallowing, of breathing, of urination and of defecation, and (4) shaken morale.

On admission to a hospital many of these patients are obviously toxic, prostrated and more or less dehydrated. The intravenous injection of moderate amounts of a 10 per cent solution of dextrose is often useful. Sister Kenny has told me that she does not like these injections because they are in the way of the essential hot foments, but she grants they are sometimes very helpful. Patients should be subjected to a minimum of handling. They are irritable and in pain, with many tender muscles, so complete rest is essential, or spasm will be increased. Examinations of the patients should, as far as possible, be limited to inspection. Spasm is sought after and, wherever found, is at once treated with hot foments according to the technic of Sister Kenny. Schwartz and Bouman have proved by their electrical recordings that under the Kenny treatment spasticity disappears and the strength of voluntary contraction improves, while without treatment spasticity does not disappear in the same time interval. Of course, nothing is permitted which may increase spasm, such as massage, electrical stimulation or splinting of any sort.

Manifestations that, in the past, have caused special trouble such as difficulties of swallowing, of breathing, of urinating, and the like, are almost always largely attributable to spasm somewhere. For instance, inability to breathe is found to be due principally to spasm of the intercostals and pectorals, or of the diaphragm, and is treated with hot foments applied more frequently and over longer periods than usual. Mechanical respirators not only interfere with this treatment but act to aggravate the spasm, although they may oxygenate the patient and give temporary relief from suffocation. Patients with moderate respiratory difficulty because of spinal involvement, those for whom the respirators have hitherto been thought to be life saving, do much better on the Kenny treatment; and patients with severe spinal involvement with so much actual paralysis of the muscles of respiration that they cannot be saved by the Kenny treatment (which naturally does not save all) would not have been saved by a respirator either, though life might have been temporarily prolonged. Patients with bulbar involvemen never have done well in respirators, so it is my sincere belief along with those who have been most closely associated with Sister Kenny that the use of the respirator is now contraindicated in the routine treatment of acute poliomyelitis. It is conceivable that a respirator may still

be valuable for keeping a patient alive until he can get the Kenny treatment, for instance during transportation to a hospital.

Disturbances of swallowing are usually due to spasm of the muscles of the neck and if treated early by the applications of hot foments around the neck are rapidly relieved. Similarly, difficulties in emptying the bowel or bladder are often quickly relieved by combating the spasm of the abdominal and lower back muscles.

For the first day or two, particularly in early cases, the application of hot foments or compresses comprises practically the entire treatment; then, when the spasm is somewhat relieved, passive motion of each involved muscle is started to establish or maintain mental awareness of its function. Fatigue and increase of spasm are sedulously to be avoided. Only when spasm and tenderness are not augmented thereby is active motion permitted and the Kenny technic of muscle reeducation fully established.

A most important part of the treatment of an early acute case of poliomyelitis is management of the morale. There are few illnesses which so greatly shake the courage of a patient's parents, and sometimes of the patient himself, as does poliomyelitis. With patients on the Kenny treatment, the maintenance of morale is easier than in former years, because the patients are more comfortable and are more hopeful from the start; but there are bound to be those destined to be left with limitations, despite the best care, and for them and their families I plead for special consideration—consideration not to take the form of extra solicitude and sympathy but rather to emphasize the distinction between restricted and handicapped. We are all of us restricted by one factor or another, whether it be by age, vision, hearing or force of other circumstance, and some have restrictions that are more obvious than others. But only those are handicapped who admit it. Surely, to be handicapped is a state of mind, a lack of courage or will or maybe of imagination. Certainly, one can recite many instances of people who have been greatly restricted but who have not been handicapped; who despite obvious limitations have fought on and conquered and who, instead of slipping into the depths, have risen to great heights. We all know of people who illustrate this point. There is the college girl who was elected president of the athletic association because she was the college champion both at archery and at canoe paddling. She had two legs that were nearly useless. A college man was awarded the most important undergraduate prize in his university because of his campus leadership. He broke the world's record in the rope climb and after graduating went on most successfully to medical school and a choice internship. He was restricted by two legs almost completely paralyzed by poliomyelitis, but he was not handicapped. A girl I know well had poliomyelitis at 14 and was left with a useless right arm and an awkward, but useful, left hand. She has gone on to graduate from high school and college with honors in campus activities as well as in her studies, has completed postgraduate instruction and holds a desirable position as a librarian. She is entirely self sufficient and well adjusted. In fact, the majority of patients with poliomyelitis usually achieve a workable philosophy; it is the parents who often need most help. Many of the paralytic, however, find most helpful the distinction between restricted and handicapped—they become willing to recognize the fact of the restrictions but press on to achieve the most with what they have.

So a great responsibility and a great privilege now belong to the pediatricians. As children stricken by this dread disease are entrusted to us, we must institute proper measures; the insuring of rest and quiet, the combating of toxicity, of spasm, and of muscle incoordination and mental "alienation" and, finally, the maintenance of morale. For thus only do we give our patients their fullest opportunity for a maximum recovery.

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SOFT PARTS DYSTOCIA

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By soft parts dystocia is meant abnormal or pathologic labor due to the soft parts of the pelvis in contradistinction to difficulties encountered because of the bony pelvis. The soft parts include the vulva, perineum, vagina, cervix, uterus, adnexa, rectum and bladder. Anomalies of any one of these structures may result in dystocia. The soft parts are much more frequently the cause of troublesome labor than the bony pelvis.

It is manifestly impossible to discuss all the disturbances of the soft parts which can give rise to abnormal labor; hence I shall limit my remarks to the important ones.

THE VULVA

The vulva is rarely the cause of dystocia, and, when it is, the pathologic condition is generally high grade edema. The latter is usually due either to toxemia or to prolonged labor with considerable vaginal manipulation, but it may be due to lymphogranuloma. Rarely the vulva may be seriously enough constricted so as to interfere with labor. Such strictures may be due to improperly performed plastic operations, burns, injuries or infections, such as syphilis or granuloma inguinale. In some instances the vulvar obstructions may be easily overcome, as for example by aspiration of fluid from highly edematous labia, but in other cases the only safe procedure for the mother is abdominal delivery.

THE PERINEUM

The perineum in primiparas is practically always a barrier to the exit of a full term baby. However, this obstruction is usually overcome by the uterine contractions with or without lacerations of the perineum, or the physician removes the barrier by manually stretching the perineum or by cutting it. Hence the perineum rarely gives any concern. Even in elderly primiparas there is seldom cause to worry about perineal obstruction. No matter how rigid the perineum may be, a sufficiently large episiotomy can practically always overcome the difficulty. The exception to this rule is the rare case of congenital or acquired narrowing which involves not only the perineum but also a good part, or all, of the vagina.

Hesitancy to employ an episiotomy has resulted in the death of some babies in cases in which there was delay at the perineum. Hence, when the second stage is prolonged, particularly when the caput is visible and still no progress is apparent, not only must the fetal heart tones be frequently auscultated to determine how the baby is tolerating labor but also an effort should be made to determine the cause of the delay. This may be

Read before the Nebraska State Medical Association, May 7, 1942.

a rigid perineum, as well as failure of rotation of the head, a narrow pelvic outlet, a short cord, a constriction ring or other cause. If the perineum seems to be delaying progress, there should be no hesitancy in performing an episiotomy. Certainly if the baby's heart tones become irregular or too rapid or too slow or if the mother is exhausted, the perineum should be incised to permit delivery of the baby. If spontaneous delivery does not follow the episiotomy, forceps should be applied.

THE VAGINA

Among the causes of vaginal dystocia are congenital narrowing and septums, constrictions due to disease, such as diphtheria in childhood, scars from trauma of labor or unskilful operations, constrictions due to burns or infections and neoplasms in or encroaching on the vagina. In most of these cases the physiologic changes which occur during pregnancy overcome the obstructions. Thus under the influence of the excessive output of estrogen during gestation the vaginal tissues soften and dilate and constrictions may disappear. Likewise during labor obstructions may vanish, particularly septums which are pushed aside and scars which are flattened out of the way of the descending baby. Only in some instances is it necessary to perform a cesarean section for vaginal dystocia or even to incise scars and septums in order to permit delivery from below. Occasionally a colpeurynter will aid in overcoming constrictions in the vagina. In other cases a deep episiotomy extending high in the vagina will help. If, however, a tumor blocks the vagina, the safest procedure is to perform a cesarean section.

THE CERVIX

The term "cervical dystocia" in my opinion is used too frequently, not because I believe the cervix is rarely responsible for trouble in labor but because the cervix is blamed in far too many cases in which the physician attempts to deliver the infant through an incompletely dilated cervix. In such a case it is not the cervix which is at fault but the impatient physician. Nevertheless there are many cases of dystocia which are attributable to the cervix.

Nearly always cervical obstructions are anatomic, but in rare cases there may be a true spasm of the external os which prevents the expulsion of the baby. A spasm may be overcome by deep anesthesia alone or by this plus digital dilatation of the cervix. Anatomic strictures of the cervix may be due to scars from previous difficult deliveries, extensive electric treatment, trachelorrhaphy and neoplasms. Likewise trouble may arise because of edema of the cervix. In addition to these definite causes there are a few disturbances of the cervix which are not well understood. Among these anomalies are adherence of the membrane to the region of the internal os preventing proper dilatation, slow and incomplete dilatation due to excessive fibrous tissue in some old primiparas and conglutination of the external os, a condition in which the cervix is completely effaced but there is absolutely no dilatation, there is practically no external os and the cervix fits the presenting part snugly.

Cervical dystocia always occurs in the first stage of labor; by definition the second stage does not begin until the cervix is completely dilated and effaced. When the second stage is reached, the cervix cannot give trouble unless edema is present. In all cases of true cervical dystocia, progress ceases at a certain point, after which the pains become increasingly stronger and more painful. In most cases the obstruction is removed by the forces of labor, but in some the physician must interfere to prevent serious damage to the mother or child, or both. If aid is not given as labor continues, the child may die, the cervix may be lacerated or torn off and expelled with the child or the lower uterine segment may rupture, with escape of the baby into the abdominal cavity.

The treatment of cervical dystocia depends on the cause. Patience coupled with ample sedation will be rewarded by spontaneous delivery in most cases, but every woman whose cervix dilates slowly in spite of strong regular contractions must be closely watched. If during a long period of time labor fails to progress because of incomplete dilatation of the cervix, seven methods are available to the physician:

1. Packing the vagina with cotton saturated with boroglycerin for a few hours often leads to dilatation of the cervix; so may a prolonged hot douche.

2. Digital dilation is helpful in some cases, but, if the cervix is rigid and only partially effaced, this is not easy to carry out. In most cases in which finger dilation is successful the cervix is lacerated, although generally the tears are small. Attempts to dilate the cervix manually should seldom be made before the cervix is completely effaced and dilated at least 7 cm. The fingers are most useful for overcoming obstruction due to edema of the anterior lip. In such cases the edematous lip can easily be pushed upward beyond the presenting part during a labor pain. Nearly always delivery follows rapidly in such cases. In a case of agglutination of the external os, if the finger is forced into the tiny opening which is usually present in the cervix it will miraculously remove this cause of dystocia. In such a case the agglutination is not complete and pressure by a finger tip causes the tiny opening to widen rapidly, so that labor is terminated quickly. The small opening can much more readily be seen through a speculum than palpated with the gloved finger. The fingers may also be used to break up adhesions between the membranes and the cervix, after which labor will progress normally.

3. Instrumental dilation with Hegar or Bossi dilators has been recommended, but these instruments should never be used during labor because they are capable of doing great harm.

4. The metreurynter may be used to overcome cervical dystocia, but there are many disadvantages to the use of rubber bags. They are foreign bodies and their presence in the lower uterine segment and vagina increases the risk of infection, they displace the presenting part with the risk of prolapse of the cord, they increase intrauterine pressure, which is hazardous in cases of distention of the lower uterine segment, they do not physiologically dilate the cervix but often produce lacerations, and nearly always when the bag is expelled, no matter how large, the cervix retracts so that its size is considerably less than the diameter of the metreurynter that slipped through it.

5. Incisions in the cervix, generally spoken of as Dührssen's incisions, are distinctly helpful in cases of cervical dystocia, but they should never be used unless the cervix is completely or almost completely effaced. If an insufficiently effaced cervix is incised there is danger of extension into the bladder, rectum or uterine arteries. Generally two or three incisions are made, at 10, 2 and 6 on the clock, and they should be long enough to permit delivery of the presenting part without undue force. Usually it is hazardous to perform version and

extraction after Dührssen's incisions because of the risk of extension of the incisions, with resultant hemorrhage and possible rupture of the uterus. Therefore, after the cervix has been incised it is best to await spontaneous delivery or deliver with forceps.

6. Vaginal hysterotomy or vaginal cesarean section should be done only by an experienced operator and only when the baby is small, particularly if the patient is a primipara.

7. Abdominal cesarean section is rarely necessary for cervical dystocia. However, if a true anatomic obstruction exists, this is the only safe procedure. If during abdominal delivery the opening in the cervix is found to be tiny, it may be advisable to amputate the uterus after the baby has been delivered. However, the necessity for a Porro operation will rarely arise, because much anatomic obstruction of the cervix is most unusual, and when it occurs it can be overcome by forcible dilation from the uterine cavity at the time of cesarean section.

In all cases of so-called cervical dystocia one must be certain the patient is actively in labor. In many cases severe uterine contractions occur during the last few days of pregnancy, yet the cervix does not dilate, the pains subside and the patient goes on for days in peace before true labor sets in. My own feeling is that regardless of how strong the uterine contractions may be, if the cervix does not become effaced, the patient is not really in labor. Such patients are having false labor pains. In most cases sedatives, such as morphine, will stop the pains. Another point of differentiation is that solution of posterior pituitary will not increase the frequency and severity of false pains. If a physician considers such a patient as having true labor pains, particularly if the contractions continue for twenty-four or forty-eight hours, and if on his own volition or because of the insistence of the patient's family that he do something he resorts to measures to hasten labor, he invites trouble. To avoid such pitfalls, the physician should use effacement of the cervix as the criterion of the presence of true labor. If the cervix is becoming effaced the patient is in labor, and if there is no effacement after a reasonable number of hours she is not in active labor.

THE CORPUS UTERI

Atony.—The body of the uterus may be the cause of dystocia in the first, second and third stages. In the first stage the most common disturbance is what is generally called atony of the uterus, although true atony does not exist. This disturbance may also occur in the second and third stages.

In the first stage atony usually manifests itself by weak and infrequent uterine contractions. Labor may drag on for days. Strong pains may occur for varying periods of time and then cease almost entirely. Dilatation and effacement of the cervix are very slow. As long as the membranes are intact there is little danger, but after rupture of the bag of waters a prolonged delay in delivery is attended with danger to the mother and baby. The chief element of risk is intrauterine infection.

Many causes have been assigned to uterine atony, including poor general health, anemia, disturbances in the nervous mechanism, fear, local alterations in the uterus, such as fibroids and scars, overdistention due to the presence of twins or polyhydramnios and malpresentation. However, in most cases the real cause of weak uterine pains cannot be found, although most likely the nervous system is at fault. In addition to the foregoing possible causes, one must always bear in mind that in many cases atony results from fatigue, that is, labor comes almost to a standstill after a prolonged period of severe uterine contractions.

The treatment of uterine atony should depend on the cause, but since in most cases this is unknown one must use certain measures which have proved to be helpful empirically. There are two main ways of treating atony, and it is highly important to choose the proper one.

In the majority of cases of uterine atony the pains at the beginning of labor are strong, and then they decrease in frequency and strength. The patient is usually tired and frightened. In these cases the best remedy is to give the patient a few hours of deep sleep. This may be secured by morphine, dilaudid, paraldehyde or any of the barbiturate drugs or by a combination of drugs, but enough should be given to insure sleep and not simply amnesia or analgesia. Nearly always, soon after the patient awakens uterine contractions begin in a normal way, and they continue to increase until delivery takes place. One must not forget to watch every patient who has atony for dehydration, starvation, a full bladder and a full rectum. Hence such a patient should be given fluids and nourishment (dextrose) in addition to sedatives for procuring sleep. Likewise, her bladder and rectum should be emptied at regular intervals. Above all, she should never be given solution of posterior pituitary or any other oxytocic to increase the strength and frequency of the pains, because she is tired physically and mentally and requires rest, not a whipping up of uterine activity. The use of oxytocics for atony may result in fetal death, rupture of the uterus and even maternal death.

In rare cases of atony in which true pains are being experienced with effacement and dilatation of the cervix, the contractions may be weak from the start and may drag on for many hours and even days. In such cases if simple measures, such as hot enemas, castor oil and quinine, do not help, solution of posterior pituitary may be used. However, only 1 minim (0.06 cc.) of the drug should be given at a time, and this should be measured in a tuberculin or similar syringe. The interval between injections should be at least twenty minutes, preferably thirty, and if pains have been initiated no more solution of posterior pituitary should be given until the pains cease. The fetal heart tones must be listened to every few minutes and certainly for at least a full minute after each injection. Furthermore, a can of ether or a bottle of chloroform should be at hand in case a too powerful uterine contraction follows an injection. I know of two ruptures of the uterus following the injection of minim doses of solution of posterior pituitary.

Atony of the uterus in the second stage of labor is usually easy to overcome. By definition the cervix is completely effaced and dilated in this stage. If the head is low down, and certainly if it is on the perineum, the baby should be delivered by means of a low forceps operation. A simpler procedure is to make an episiotomy and use the Kristeller expression to deliver the baby; but this procedure must be carried out with the utmost care to avoid traumatizing the uterus and placenta and to prevent injury to the baby. Of course, the Kristeller expression should never be attempted if the lower uterine segment is thinned out. Occasionally when the head is on the perineum it can be delivered by a modified Ritgen maneuver; that is, pressing the head out by means of the fingers placed on either side of the anus. This procedure is especially successful if combined with an episiotomy. If the head is high up

after the cervix is fully dilated, delivery should be accomplished by version and extraction.

I prefer these methods of delivery to the use of solution of posterior pituitary, which is especially dangerous in the second stage of labor. The only indication for this drug in the second stage of labor is when the head is on the perineum and there is no disproportion. Even in such a case I should resort to a low forceps operation because I can always control the instrument but not always the drug.

Uterine atony in the third stage usually results in hemorrhage. The treatment of this consists in uterine massage, removal of the placenta and membranes if they are still in utero, the intravenous injection of ergonovine, the intramuscular injection of solution of posterior pituitary, intrauterine packing and, when necessary, blood transfusions or the use of plasma or serum. I have found the injection of solution of posterior pituitary directly into the uterine muscle through the abdominal wall to be a highly effective method of controlling bleeding, but this procedure should be carried out only by an experienced physician.

Uterine Tetanus and Spasm.—Dystocia may be produced not only by uterine atony but also by the reverse; namely, excessively severe uterine contractions. When the entire uterus is involved in the process the condition is spoken of as uterine tetanus. When only a localized area of the uterus is contracted, the condition is described as uterine stricture. The most likely cause of these disturbances is a disturbance in the nervous mechanism of the uterus. Spasms of the uterine musculature may be brought about by local manipulation, such as rough examinations, forcible dilation of an incompletely dilated cervix, intrauterine manipulation, attempt to deliver a baby through an incompletely dilated cervix and obstructed labor. Solution of posterior pituitary may also cause these anomalies.

When there is a tetanic contraction of the uterus, be it general or local, labor ceases. Both the mother and the baby, however, suffer considerably. The maternal and fetal mortality and morbidity are very high, particularly in the cases of conditions to be described as constriction rings.

Clinically the most important type of stricture of the uterus and the one which gives the most trouble is that known as Bandl's ring. The terminology of this condition is most confusing; hence a word of explanation. Situated between the body of the uterus and the lower uterine segment is a distinct area all around known by various names, such as the constriction ring of Schroeder and the retraction ring of Barbour and Lusk. However, Rudolph and Ivy properly suggested the name physiologic retraction ring for this area. This ring is usually at the level of the symphysis pubis and is at about the region where the anterior uterine peritoneum is fixed to the uterus. In contradistinction to the physiologic retraction ring is the Bandl ring, which is called the pathologic retraction ring by Rudolph and Ivy. This is usually situated about 14 to 16 cm. above the superior border of the symphysis pubis or in the region of the umbilicus. It may be identified as an oblique or transverse depression in the anterior abdominal wall. It is distinctly palpable when a hand is inserted into the uterine cavity, and this is the only way to make an absolute diagnosis of pathologic retraction ring. Whenever such a ring is present one must be on guard against a rupture of the uterus, because the lower uterine segment is usually elongated and thin; on the other hand, the corpus is thicker.

In a woman with a pathologic retraction ring the uterine contractions are very painful, but in spite of this there is no progress in labor. The delay in labor is usually erroneously ascribed to cervical dystocia, occiput posterior or disproportion.

Abdominal examination in a case of Bandl's ring usually reveals the groove as described. On rectal examination it will be found that in spite of strong and regular pains the cervix is not fully dilated, that it is soft and edematous and that the head does not seem to fit the pelvic cavity. On vaginal examination the soft, succulent, incompletely dilated cervix can be felt and also the head, which does not come down to fill the lower uterine segment during a uterine contraction. Insertion of the hand into the uterine cavity easily reveals the tense ring all around the uterus. Bandl's ring may, of course, develop in the second stage of labor, and in such a case either the head comes down almost to the perineum during each contraction and immediately recedes or it does not come down very far with the pains. A localized spasm may occur in the third stage of labor and interfere with placental separation.

The preparation of the patient's psyche for labor may prevent the development of Bandl's ring in some cases, especially in women who are unduly apprehensive about childbirth. Likewise, the avoidance of oxytocics, rough vaginal examinations, unnecessary intrauterine manipulations and forcible dilation of the cervix will definitely diminish the incidence of pathologic retraction rings. The proper use of sedation will prevent the condition in a few more cases.

If the diagnosis is made during the first stage, large doses of sedatives should be given in order to secure rest for the uterus and sleep for the patient. If this plus repeated bolstering of the patient's psyche by encouragement and fortification of the patient's physical condition by means of fluids and dextrose do not result in progress after a long lapse of time, delivery must be accomplished. Sometimes, when the patient is in excellent physical condition, when the vaginal examination was performed gently and without risk of infection and when the baby is in good condition, cesarean section should be performed, preferably the cervical type and under local anesthesia. In other cases, if the head is fairly low down and the cervix completely dilated, the Bandl's ring may be gently but steadily dilated under deep anesthesia and the baby delivered by forceps. Ether and chloroform are the best anesthetics for this purpose. If difficulty is encountered under deep anesthesia, 8 minims (0.5 cc.) of epinephrine should be given hypodermically, as advocated by Rucker. This treatment often results in relaxation of the ring. If the head is high and the ring can be dilated, version and extraction may be performed, provided the lower uterine segment is not thinned out. In some cases it will be necessary to dilate the cervix manually before delivery by forceps or version can be accomplished. If the baby is dead, and in some cases in which it is alive, the application of a Willett forceps or a volsellum to its scalp with an attached weight will result in spontaneous delivery. In some cases when the baby is dead craniotomy must be done. When all manipulations from below fail to bring about delivery of the baby a Porro operation must be done, but this will rarely ever be necessary if proper judgment and average skill are used. In some cases an extraperitoneal cesarean section, such as the one described by Waters, will enable the operator to save the uterus.

Other Causes of Uterine Dystocia.—Another disturbance of the uterus which may result in dystocia is the presence of myofibromas. Fortunately in most cases these growths give very little trouble during labor. Sometimes they cause irregular contractions in the first stage; occasionally they produce malpresentations, and not infrequently they result in hemorrhage in the third stage and infection in the puerperium. Rarely they block the exit of the child, making cesarean section imperative.

Still another uterine source of dystocia is the presence of a scar from a previous cesarean section. Regardless of the type of cesarean section performed there is always some risk of rupture in a subsequent pregnancy and labor. After the classic operation many ruptures have occurred not only during labor but also in pregnancy while the patient was at rest. However, after the cervical cesarean section, rupture during pregnancy is extremely rare and rupture during labor is far less common than after the classic operation. Regardless of this, every woman who has had a cesarean section should give birth to all her subsequent babies in a hospital. If the same indication for cesarean section exists as for the first operation, for example a contracted pelvis, of course the operation should be repeated, preferably a few days before term or as soon after the onset of labor as possible. However, if the indication for the first cesarean section, i. e. placenta previa or severe toxemia, is not present subsequently, the patient may be permitted to deliver from below, but only in a hospital. If vaginal delivery is to take place it is safest to deliver the baby by low forceps soon after the cervix is completely dilated. If there is good reason to believe that the cesarean scar did not heal properly, as may occur after a markedly febrile puerperium, or if a defect is definitely felt through the abdomen, an elective cesarean section should be performed a week or ten days before term.

Scars from myomectomy operations need not be feared, because a rupture of such a scar in labor is a great rarity.

THE ADNEXA

Practically the only way the adnexa can result in dystocia is by the development of a tumor. The most frequent neoplasm of obstetric interest is an ovarian cyst, regardless of whether it is a simple serous cyst, a dermoid, carcinoma or other type. The only consideration is whether the growth is large and obstructs the exit of the child. Otherwise it has practically no obstetric importance unless it undergoes torsion. If acute torsion occurs an operation must be performed, whether this takes place in pregnancy, labor or the puerperium. Ovarian cysts give rise to dystocia much more frequently than do uterine fibroids; hence some obstetricians believe that every ovarian neoplasm discovered during pregnancy should be removed. However, I have followed many women with ovarian cysts during pregnancy, labor and the puerperium without observing any harm. Hence I believe that if an ovarian tumor is drawn up out of the pelvic cavity during pregnancy and does not block delivery of the baby it should be left alone. If, however, an ovarian cyst remains in the cul-de-sac and cannot be displaced by posture and gentle pressure, it should be removed, preferably during pregnancy. If there is reason to suspect malignancy of an ovarian tumor or if a roentgenogram reveals a dermoid cyst, an operation should likewise be performed.

FULL BLADDER AND RECTUM

Occasionally an overdistended bladder or an overloaded rectum will interfere with the progress of labor. For this reason it is important to be sure the patient empties her bladder and rectum or that these organs are emptied by catheter and enema respectively whenever these procedures seem necessary.

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PITRESSIN TANNATE IN OIL IN THE TREATMENT OF DIABETES INSIPIDUS

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The effects and disadvantages of solution of posterior pituitary and of pitressin administered hypodermically or intranasally in relieving the symptoms of diabetes insipidus are well known. The subcutaneous injection of the drug causes local irritation and is frequently followed by intestinal cramps, diarrhea, headaches, palpitation and pallor. Moreover, the therapeutic effect is temporary, lasting only a few hours. In order to control a patient's symptoms by this method, it is necessary to inject the drug three, four or more times a day. The intranasal use of solution of posterior pituitary and of pitressin appears to be somewhat more satisfactory because it avoids the necessity of injection and can be taken easily a number of times a day. Again, however, the effect lasts only for several hours. Frequently patients become sensitive to the drug intranasally with resultant sneezing, irritation of the nose and a mucous discharge and diminished absorption.

A compound solution of posterior pituitary with slow absorption and a greatly prolonged antidiuretic effect appears desirable, especially if there are no side reactions. Green and January [1] found that pitressin tannate in oil given subcutaneously to 3 patients with diabetes insipidus had an antidiuretic effect for thirty to eighty-two hours. In Stephens's [2] cases, single injections of this preparation exhibited an antidiuretic effect for twenty-four to ninety-six hours. Thorn and Stein [3] observed that the intramuscular injection of pitressin tannate in oil was very effective in 3 cases of diabetes insipidus and that the symptoms were controlled for twenty-four to forty-eight hours. It appears that pitressin tannate in oil, administered hypodermically, has an antidiuretic effect in cases of diabetes insipidus which may last for twenty-four to ninety-six hours.

This paper reports the results in 8 cases of diabetes insipidus following the subcutaneous or intramuscular injection of pitressin tannate in oil.[4]

The plan of study consisted chiefly in observing the daily fluid intake and output before and after the hypodermic injection of pitressin tannate in oil. In addition,

From the Medical Clinic of the Peter Bent Brigham Hospital.

1. Green, J. A., and January, L. E.: Diabetes Insipidus Treated by the Subcutaneous Administration of a Suspension of Pitressin Tannate in Oil, J. A. M. A. **115**: 1183 (Oct. 5) 1940.
2. Stephens, D. J.: Pitressin in Oil: Prolonged Antidiuretic Effect in Experimental and Clinical Diabetes Insipidus, J. Clin. Investigation **20**: 463, 1941.
3. Thorn, G. W., and Stein, K. E.: Diabetes Insipidus and Pitressin: Pitressin Tannate Therapy in Diabetes Insipidus, J. Clin. Endocrinol. **1**: 680 (Aug.) 1941.
4. Pitressin tannate is a water insoluble chemical combination of the pressor fraction of the posterior lobe of the pituitary gland with tannic acid. The pressor fraction is precipitated with tannic acid and the precipitate is removed by filtration, washed and dried under aseptic conditions. Five pressor units of pitressin tannate is suspended in 1 cc. of peanut oil. The pitressin tannate in oil was supplied by Parke, Davis & Co.

the weight of the patients and the specific gravity of the urine were noted frequently. Various blood tests were made in certain instances. In all of the cases 1 cc. of pitressin tannate in oil was injected subcutaneously or intramuscularly daily for several days and then on

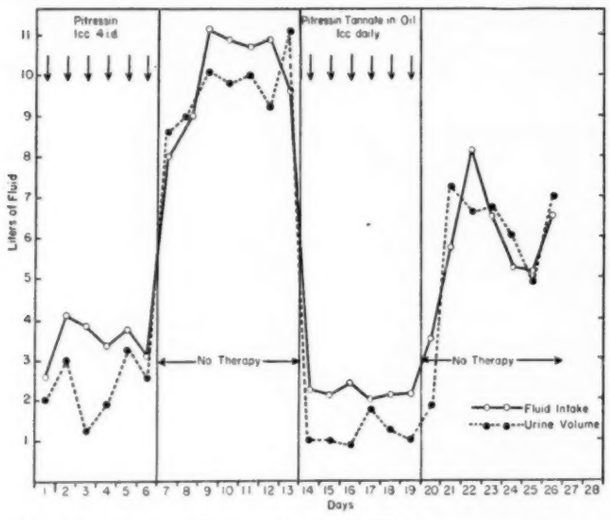

Chart 1.—Relative effects of pitressin, pitressin tannate in oil and no treatment on the daily fluid intake and output of a patient (Mr. H. N.) with diabetes insipidus.

alternate days or at longer intervals. The longest period of administration of the drug in these cases was seven months.

CLINICAL MATERIAL AND RESULTS

The persons studied included 5 males and 2 females who had had diabetes insipidus of idiopathic origin for a number of years and 1 male whose diabetes insipidus was due to a brain tumor. Except for the last person, I have observed the cases for three or ten years and know well the state of their disease. The ages of the males ranged from 14 to 37 years and the ages of the women were 29 and 72 years. All were relieved of the polyuria and polydipsia with the intramuscular or intranasal administration of solution of posterior pituitary except the patient with brain tumor.

REPORT OF CASES

The cases are presented briefly as follows:

CASE 1.—H. N., a man aged 37, unmarried, had had diabetes insipidus for seventeen years. His general physical examination was normal, although he was about 10 pounds (4.5 Kg.) underweight. His daily fluid intake and output usually varied from 10 to 11 liters. With 1 cc. of pitressin injected four times a day, his daily fluid intake and output were about 2 to 4 liters. When 1 cc. of pitressin tannate in oil was injected daily, the fluid intake dropped to approximately 2 liters and the urine volume to about 1 liter a day. When the drug was omitted for four or five days the fluid intake and output had increased but not to the large volumes which were present before this therapy was started. After four days of treatment with the drug he put on 3 pounds (1.3 Kg.). The details of his fluid intake and output are recorded in chart 1. Later the drug was administered every other day and the fluid intake and output remained at about the level when the drug was given each day.

CASE 2.—Miss E. S., a school teacher aged 29, had had polyuria and polydipsia for eleven years. Her daily fluid intake and output had been about 10 or 11 liters. The menstrual history had been normal, but the intramuscular injection of solution of posterior pituitary caused dysmenorrhea. One cc. of solution of posterior pituitary injected three times a day or the intranasal insufflation of powdered pituitary about eight or ten times a day reduced the daily fluid intake and output to about 3 liters. The physical examination was negative, but she was about 15 pounds (6.8 Kg.) underweight. The administration of 1 cc. of pitressin tannate in oil, daily and on alternate days, reduced her daily intake and output to a very low level, usually between 500 and 1,000 cc. The details of her fluid intake and output are shown in chart 2. Here again the fluid intake and output increased considerably after the drug had been omitted for six days but not to the high levels present before therapy. No painful menses occurred during this treatment.

CASE 3.—F. C., a man aged 36, married, a clerk, developed diabetes insipidus during the course of a severe septic sore throat twelve years previously. His daily fluid intake and output during the past four or five years had been about 9 liters. He was unable to use solution of posterior pituitary intranasally because it produced asthmatic attacks. The physical examination was normal. The administration of 1 cc. of pitressin tannate in oil every sixty hours kept his daily fluid intake and output at approximately 1 liter.

CASE 4.—J. K., a man aged 30, a clerk, had had polyuria and polydipsia for eleven years. His daily fluid intake and output had been as high as 11 liters in the past and about 6 liters during the last three or four years. The physical examination showed him to be about 15 pounds (6.8 Kg.) underweight. The skin was of the female type and he was sexually underdeveloped. The administration of 1 cc. of pitressin tannate in oil every other day reduced his fluid intake and output to approximately 0.5 to 1 liter a day.

CASE 5.—A. S., a man aged 27, unmarried, a musician, had had the disease for sixteen years with a daily fluid intake and output of about 14 liters. This was reduced to 3 or 4 liters when 1 cc. of solution of posterior pituitary was injected three

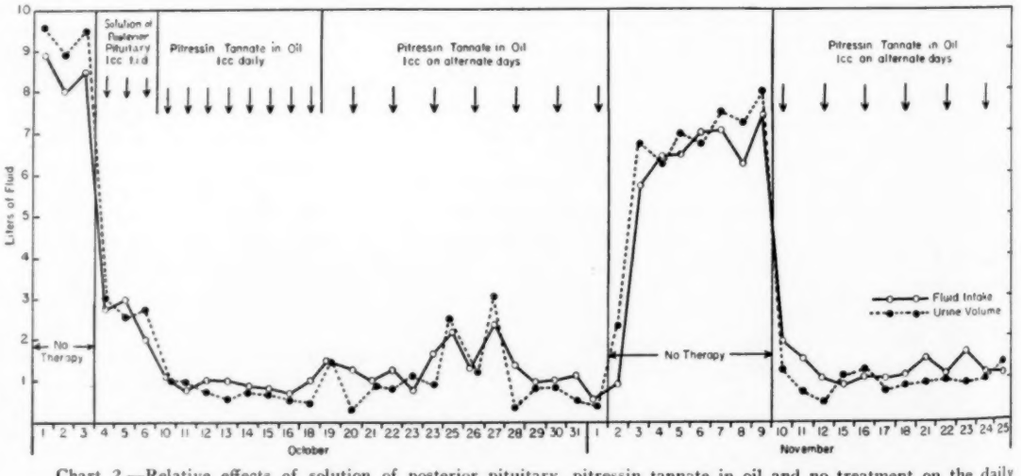

Chart 2.—Relative effects of solution of posterior pituitary, pitressin tannate in oil and no treatment on the daily fluid intake and output of a patient (Miss E. S.) with diabetes insipidus.

times a day. The physical examination was entirely normal. The administration of 1 cc. of pitressin tannate in oil on alternate days reduced the daily fluid intake and output to about 2 liters a day.

CASE 6.—Mrs. M. A., aged 72, a housewife, had had diabetes insipidus for eleven years. She had had eight children and had gone through the menopause about twenty-five years

previously. Her daily intake and output had been about 10 liters. She had a total thyroidectomy on June 24, 1935, and the details of this aspect of the case were published elsewhere.[5] The essentials of the recent examination were obesity, moderately enlarged heart and slight edema of the legs. Her height was 5 feet (152 cm.) and her weight 198 pounds (90 Kg.). The pulse rate was 72. The basal metabolic rate was — 10 per cent. Her daily intake and output had been about 10 liters until a year ago, when it dropped to about 6 liters. Five-tenths cc. of solution of posterior pituitary administered intranasally three or four times a day reduced the values to approximately 2 or 3 liters a day. The injection of 1 cc. of pitressin tannate in oil every other day kept the fluid intake and output at approximately 1 liter.

CASE 7.—G. A., a boy aged 14 years, had had polyuria for five and one-half years with a daily fluid intake and output of approximately 10 liters. He had been maturing sexually during the previous three months. The physical examination was normal. The fluid intake and output had been about 3 liters on 25 mg. of powdered pituitary taken by insufflation four times a day. The daily administration of 1 cc. of pitressin tannate in oil for several days reduced the daily fluid intake and output to slightly less than a liter, beginning with the first injection. When the drug was given on alternate days, the volumes rose to approximately 3.5 liters on the day it was not used.

CASE 8.—R. M., a man aged 29, single, an electrician, was found to have a neoplasm of the third ventricle of unknown type in October 1932 and had received roentgen therapy for this. For the past six months he had had some polyuria. However, during the previous week he developed great thirst and frequency and said that his intake was about 8 liters a day. His general physical examination was not remarkable except for some neurologic changes due to the brain tumor. His spinal fluid contained 107 mg. of protein per hundred cubic centimeters. At the hospital his fluid intake ranged from 4,350 to 5,950 cc. and the output from 4,200 to 5,760 cc. without therapy. On 1 cc. of solution of posterior pituitary injected twice a day his fluid intake ranged from 4,300 to 7,200 cc. and the output from 3,300 to 6,700 cc. With the daily injection of 1 cc. of pitressin tannate in oil the fluid intake ranged from 3,200 to 2,400 cc. and the output from 1,100 to 1,950 cc.

COMMENT

The hypodermic administration of 1 cc. of pitressin tannate in oil was very effective in reducing the fluid intake and output to normal in these cases. The effect of the first injection of the drug was so evident that the subsequent twenty-four hour fluid intake and urine volume were normal. When injected daily its antidiuretic effect became cumulative and these volumes decreased to below the average normal. The antidiuretic effect usually was as obvious during the second twenty-four hours as it was during the first twenty-four hours after the injection of the drug. Consequently the frequency of the use of 1 cc. of this medication was adjusted so that it was given every forty-eight or sixty hours. With this adaptation the fluid intake was near normal and the polyuria, polydipsia and thirst completely disappeared. In the case of brain tumor the duration of action of the drug was only about thirty hours, but in this case standard solution of posterior pituitary had no effect. This was the only case in which the drug was needed daily.

It was interesting that the patients commented that pitressin tannate in oil increased the saliva and improved the appetite and digestion. Also the dryness in the mouth, which occurred even with solution of posterior pituitary therapy, disappeared. There were no disagreeable side reactions such as local irritation, slough, pallor or intestinal cramps. Nevertheless 4 of the 8 patients have discontinued the use of pitressin tannate in oil because they can take pituitary intranasally and avoid injections.

There was no significant change in the body weight after administration of pitressin tannate in oil with the dose used except in 1 case, in which 3 pounds (1.3 Kg.) was gained after four days of the daily injection of the drug. The specific gravity of the urine, which was usually 1.001 or 1.002, increased to 1.026 and even 1.030 with pitressin tannate in oil therapy.

The hematocrit and phenolsulfonphthalein excretion were determined before, during and after treatment with pitressin tannate in oil in 1 case. The phenolsulfonphthalein excretion remained the same during the various periods of observation, being approximately 68 per cent in one hundred and thirty minutes. The blood showed slight dilution, as evidenced by the hematocrit of 42 per cent without treatment and 38 per cent during therapy.

SUMMARY

Some observations were made on the effect of hypodermic injections of 1 cc. of pitressin tannate in oil on the daily fluid intake and output of 8 patients with diabetes insipidus. It usually was administered daily for several days and then on alternate days.

The duration of its action in controlling the polydipsia and polyuria was forty-eight to sixty hours in 7 cases of diabetes insipidus of idiopathic origin and thirty hours in 1 case in which the polyuria was refractory to solution of posterior pituitary and due to a brain tumor. There were no appreciable changes in the body weight or toxic reactions with the dose and frequency of the administration of the drug in these cases.

The fluid intake and output of patients with diabetes insipidus was maintained at a normal level with pitressin tannate in oil more consistently and satisfactorily than with any other drug.

189 Bay State Road.

5. Blotner, Harry, and Cutler, E. C.: Total Thyroidectomy in the Treatment of Diabetes Insipidus, J. A. M. A. **116**: 2739 (June 21) 1941.

Bird Preserves.—There are five large national organizations of bird lovers: the American Ornithological Union with a membership of 1,800, composed chiefly of professional people (educators, scientists, lawyers), the National Audubon Society with 6,300 adult members and more than 200,000 school children in the Junior Audubon Clubs, the Wilson Ornithological Club and the Cooper Ornithological Club, each with over 1,500 members, and the bird banding organizations, of which there are four with interrelationships among them. . . . The National Audubon Society does not limit its interest entirely to birds, and since its organization in 1885 it has been one of the most powerful forces for conservation of wild life in this country. It was largely responsible (during the term of President Theodore Roosevelt) for starting bird preserves, of which the federal government has established about one hundred and seventy, covering approximately 14,000,000 acres. The Audubon Society itself maintains protection on 5,000,000 acres in thirty-six different areas, and most of the states have set aside preserves amounting to several thousand in number. The largest preserve, set aside by Taft, is in the delta of the Yukon, an area larger than the state of Connecticut. In 1913 President Wilson established the Panama Canal as a bird refuge. There are countless private bird preserves. As a result of these efforts undoubtedly the smaller birds are more numerous in this country than ever before.—Menninger, William C.: Bird Study, *Bull. Menninger Clin.* **6**:93 (May) 1942.

THE ACUTE TOXICITY OF MERCURIAL DIURETICS

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Several human fatalities have recently been reported for which the intravenous injection of a mercurial diuretic was believed to be the causative agent.[1] It therefore seemed desirable to make a comparison of toxicity of the mercurial diuretics by this route and to study the influence of the drugs commonly used in the treatment of heart disease on this toxicity. The drugs used for the comparison were esidrone, mercupurin and salyrgan-theophylline and the three parent mercurials, esidrone without theophylline, mercurin and salyrgan.

PROCEDURE AND RESULTS

Comparative Acute Lethal Dose.—The cat was selected as the experimental animal. The drugs were injected without dilution so that the concentration of mercury was approximately 40 mg. per cubic centimeter in every case. Injections were given into the femoral vein by means of a micro buret connected to a 19 gage needle with a short piece of rubber catheter. No anesthesia was used and conditions thus approximated those which obtain clinically. It seemed probable that the rate of injection might modify the magnitude of the lethal dose and therefore a scheme similar to the proposed U. S. P. XII cat assay for digitalis was adopted. An amount (one tenth to one fifteenth of the lethal dose determined by preliminary experiments) of drug was injected per kilogram every two minutes, so that death should occur between twenty and thirty minutes after the start of the injections. This time interval was made as short as possible so that the lethal action of the drug would be limited to the acute phenomena observed in man. It is recognized that a single injection with the observation of death or survival would be even more applicable, but such a quantal response technic would require a prohibitive number of animals to obtain the same precision as in the method just described. Medium size healthy cats were assigned by lot to the drugs listed in table 1. Excepting esidrone without theophylline, and theophylline sodium acetate, the assays were run in parallel, 2 cats being killed for each of the five drugs on each of three days. The results are thus not biased by a secular trend in the sensitivity of the animals.

The results of the assay of the diuretics are given in table 1 together with other pertinent information. The lethal doses are expressed in cubic centimeters of ampule solution per kilogram and are adjusted on the basis of chemical analysis to an equal mercury concentration of 40 mg. per cubic centimeter. It will be seen that esidrone was the most toxic drug either with or without theophylline; salyrgan is intermediate and mercupurin, mercurin and salyrgan-theophylline are the least toxic.

Comparison of Mercupurin and Salyrgan-Theophylline.—These drugs are the only mercurial diuretics that are available to the physician at the present time. It is therefore important to decide whether or not there is a significant difference between the mean lethal dose of 0.83 cc. per kilogram for mercupurin and 1.11 cc. per kilogram for salyrgan-theophylline. For this purpose t was calculated according to Fisher and found to be 1.93, which fails to exceed the expected value of 2.228 for odds of 20 to 1. Thus, there is better than one chance in twenty that the difference between these two mean lethal doses might have occurred by random sampling alone, and by the usual criteria the difference would not be considered significant.

Influence of Theophylline.—Theophylline was originally added to these drugs because it was shown to enhance their absorption and lessen their local toxicity. It will now be seen that (table 1) theophylline also lowers the acute intravenous toxicity in the case of salyrgan and mercurin, although it fails to modify the toxicity of the esidrone mercurial base. It was previously demonstrated[2] that theophylline increases the

TABLE 1.—*Composition and Lethal Dose of Mercurial Diuretics in the Cat*

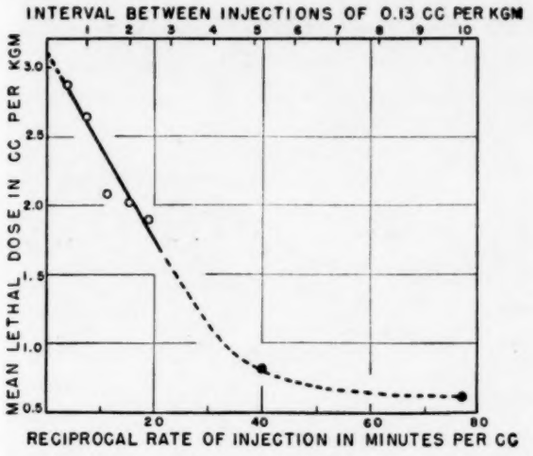
Drug	Mercupurin	Mercurin	Salyrgan-Theophylline	Salyrgan	Esidrone	Esidrone Without Theophylline	Theophylline Sodium Acetate
Volume in cc. per Kg. injected at two minute intervals	0.05	0.05	0.1	0.1	0.02	0.02-0.04	0.5
Mercury content, mg. per cc. by analysis	42.5	36.1	40.2	40.8	43.2	40.2	None
Labeled anhydrous theophylline content, mg. per cc.	35.3	None	45.5	None	39.6	None	34.4
Lot number	411876	E 2249	GE 857	FP 858	91663	Prepared in this laboratory	Prepared in this laboratory
p_H (glass eletrode)	8.6	8.7	7.8	9.2	8.0	10.4	9.5
Lethal dose in cc. ampule solution per Kg. when injected at a rate which killed in 20 to 30 minutes (adjusted to a mercury content of 40 mg. per cc.)	0.85 0.48 0.75 0.79 1.33 0.78	0.28 0.87 0.40 0.68 1.05 0.94	1.41 1.00 1.00 0.97 1.39 0.90	0.87 0.32 0.39 0.26 0.31 0.33	0.29 0.27 0.21 0.23 0.16 0.32	0.19 0.20 0.31 0.30 0.36	5.5 7.0 5.0
Mean lethal dose	0.83	0.70	1.11	0.41	0.24	0.27	5.8
Average time of death in minutes	31	31	22	20	22	24	23

From the Department of Therapeutics, New York University College of Medicine.

1. Friedfeld, Louis; Kissin, Milton; Modell, Walter, and Sussman, Ralph: Mercupurin, correspondence, J. A. M. A. **117**: 1806 (Nov. 22) 1941.

2. DeGraff, A. C.; Batterman, R. C.; Lehman, R. A., and Yasuna, E.: Proc. Soc. Exper. Biol. & Med. **39**: 250 (Nov.) 1938.

maximum rate of urinary excretion of salyrgan to a greater extent than mercurin and causes both maximums to occur somewhat earlier. From table 1 it appears that theophylline lowers the toxicity of salyrgan to a greater extent than mercurin, and it seems logical to surmise that the onset and rate of excretion of mercury



Linear relationship between reciprocal injection rate and mean lethel dose for mercupurin in the cat.

following injection of these mercurials is an important factor in determining their lethal dose in the cat. Since the lethal dose of theophylline itself by this technic is about six times as large as the least toxic mercurial, it is unlikely that this substance makes any considerable contribution to the lethal effect. The action of the theophylline is most probably the result of a chemical combination with the mercurial, as was shown for its other effects.[3] There is, of course, no way to determine whether the lethal doses found in this study for the cat stand in the same relationship to each other as they do for man. However, deaths were reported a few months after the marketing of esidrone but were observed only after several years of clinical use of salyrgan and mercupurin. This would lend credence to the assay results, since esidrone was found to be much more toxic than mercupurin or salyrgan.

Influence of Other Drugs on the Lethal Dose of Mercupurin.—Various drugs are used in the treatment of heart disease concomitantly with the mercurial diuretics, and it seemed possible that one of them might, by sensitization of the heart, or in some other way, precipitate the fatal syndrome. Furthermore, the rate of injection will control the concentration of mercury to which the tissues are at any time exposed. These two factors were studied simultaneously, a randomized 5 by 5 Latin square design being used. This procedure has been described in detail by Fisher [4] and others and has the advantage of efficiency in the use of the animals and in evaluating the interaction of the variables. In this study mercupurin was used as a typical mercurial diuretic and was injected in doses of 0.13 cc. per kilogram. Five cats were killed on each of five days. On any given day 1 cat was killed by repeated injections at each of the following five time intervals: 0.5, 1.0, 1.5, 2.0 and 2.5 minutes corresponding to reciprocal injection rates of 3.8, 7.7, 11.5, 15.4 and 19.2 minutes per cubic centimeter. At the same time that rates of injection were varied on different days there were five preliminary treatments given, as here listed. The doses per kilogram are as nearly as possible equal to the maximum which would be used clinically.

A. Digitaline Nativelle: This was administered intravenously twenty-four hours before the assay at a dose of 0.025 mg. per kilogram, or about one-sixteenth the average lethal dose.

B. Aminophylline: Fifteen minutes before the assay, 4.8 mg. per kilogram was injected intravenously.

C. Ammonium Chloride: One hour before the experiment, 20 mg. per kilogram was administered orally in a red gelatin capsule. The animals were put into individual cages and observed carefully, and whenever there was evidence of emesis the animal was taken out of the series and another substituted.

D. Untreated control.

E. Soluble Phenobarbital: One hour before the assay, 20 mg. per kilogram was given orally in a capsule and the same precautions taken as in C against loss of the drug by emesis.

The lethal doses in cubic centimeters of ampule solution per kilogram are given in table 2. In table 3 the analysis of variance for these data is given in the usual form so as to test the significance of the various factors. The conclusions from this experiment are that (1) there was no significant modification of the lethal dose either because of determinations on different days or (2) as the result of treatment with other drugs commonly used in heart disease.[5] On the other hand, there was (3) a highly significant linear relationship between the interval between injections and the lethal dose. This relationship is shown graphically in the chart. It will be seen that the longer the interval between injections (or the longer the length of time required for injection of 1 cc.), the smaller the lethal dose. However, after about forty minutes per cubic centimeter the curve flattens but will undoubtedly rise again when the intervals become so long that excretion becomes a major factor. The implication is that these mercurials have a slightly delayed action and that injecting them in man at an unusually slow rate would give no guaranty that a reaction would not occur. It may be noted from the chart that the point plotted at 0.83 cc. per kilogram and forty minutes per cubic centimeter is taken from table 1. Thus it appears that (at least in the case of mercupurin) the lethal dose determined over a twenty to thirty minute period actually approaches a minimum average lethal dose under the conditions described.

TABLE 2.—*Influence of Preliminary Treatments and Injection Intervals on the Lethal Dose of Mercupurin in Cubic Centimeters per Kilogram*

Treatments are designated A, B, C, D and E and are described in the text.

Date of Experiment	Interval Between Injection of 0.13 Cc. per Kg.				
	0.5 Min.	1.0 Min.	1.5 Min.	2.0 Min.	2.5 Min.
December 3	1.30 C	1.43 A	1.30 D	1.17 E	0.65 B
December 4	1.95 D	1.17 B	1.30 E	1.04 C	1.04 A
December 5	1.82 B	1.30 C	1.30 A	1.04 D	0.91 E
December 8	1.69 A	1.43 E	0.52 C	0.91 B	0.91 D
December 9	0.78 E	1.30 D	1.04 B	0.91 A	1.04 C

3. Lehman, R. A., and Dater, A.: J. Pharmacol. & Exper. Therap. **63**: 443 (Aug.) 1938. DeGraff, A. C.; Baterman, R. C., and Lehman, R. A.: Proc. Soc. Exper. Biol. & Med. **38**: 373 (April) 1938.

4. Fisher, R. A.: The Design of Experiments, ed. 2, London, Oliver and Boyd, 1937.

5. It is recognized, however, that long continued treatment with digitaline Nativelle can cause myocardial damage in the cat and ammonium chloride depletion of base. Hence the single doses used here do not exhaust the possibility of a synergistic effect on the mercurial diuretics.

Effect of Dilution.—Since the maximum effect of these mercurials comes on only after a delay of some minutes, dilution would not be expected to have any considerable effect. This is shown in table 4. The mercupurin ampule solution was diluted with isotonic solution of sodium chloride as indicated and approximately one lethal dose (0.83 cc. per kilogram) was injected over a period of twenty seconds in each case. There is some indication that the drug is less toxic when highly diluted. Nevertheless, 1 animal out of 3 died at a dilution of 25 to 1, so that this would not seem to offer any practical solution to the problem of human fatalities.

Mechanism of the Lethal Action.—In order to determine whether or not the circulatory action of the mercurial diuretics used in this study is qualitatively the same as that of other mercurials whose actions have been reported in the literature, various experiments were carried out on the cat under pentobarbital anesthesia. Measurements were made of the mean carotid blood pressure, venous pressure, respiration, electrocardiogram and intestinal and hind limb volume after intramuscular and repeated intravenous injections of several of the diuretics used. The evidence obtained is in agreement with previous reports and indicates that death is primarily the result of the cardiac action of mercury. The organic residue unquestionably modifies the magnitude of the lethal dose but does not appear to cause any qualitative change in the fatal sequence of events.

If the mercurial is introduced into the blood stream rapidly, the heart may suddenly go into ventricular fibrillation and continue to fibrillate for several minutes after the blood pressure has fallen to zero and the

TABLE 3.—*Analysis of Variance for Factors Affecting the Lethal Dose of Mercupurin (Data of Table 2*)*

Variation Due to	Degrees of Freedom	Sum of Squares	Variance	Variance Ratio	Interpretation
Assumption of a linear relationship between the lethal dose and the injection interval (reciprocal rate)	1	0.137,770	0.137,770	9.24	Odds are about 100 to 1 against this value occurring by random sampling
Assumption of a curvilinear relationship for the above	3	0.008,467	0.002,822	< 1	The variances for these factors are less than the experimental error and thus do not approach significance
Preliminary treatments	4	0.040,945	0.010,236	< 1	
Change in the sensitivity of cats on different days	4	0.045,748	0.011,437	< 1	
Experimental error (uncontrolable factors)	12	0.179,073	0.014,923	1	
Total.....	24	0.412,002			

* The lethal doses of table 2 were changed before the analysis to logarithms, since this function usually is more normally distributed than is the dose in cubic centimeters per kilogram.

respirations have ceased. With more gradual administration of the drug (either intravenously or by a large dose intramuscularly) the electrocardiogram shows T wave changes followed by an intraventricular block. These effects are accompanied by a gradual fall in the arterial and venous pressures and an equivalent fall in the volume of the intestine and the leg. As more drug is injected intravenously or absorbed from the muscle, a rapid ventricular tachycardia usually ensues, the blood pressure fluctuates in a highly irregular manner between about 10 and 40 mm. of mercury and the venous pressure rises sharply. This state may terminate in one of the following ways: (1) The respiration fails, presumably owing to anoxia resulting from

TABLE 4.—*Effect of Dilution of Mercupurin on the Lethal Effect*

Approximately one lethal dose (0.83 cc. per kilogram) given in twenty seconds

Cat	Dilution	Result
1.....	5 times	Died in 10 minutes
2.....	5 times	Died in 8 minutes
3.....	5 times	Survived
4.....	12 times	Died in 18 minutes
5.....	25 times	Died in 20 minutes
6.....	25 times	Survived
7.....	25 times	Survived

the low blood pressure; (2) death results from ventricular fibrillation, or (3) the heart recovers to a slow sinus rhythm with an intraventricular block and the blood pressure rises. Mercuric succinate, mercury bichloride, salrygan and neptal have been studied by Salant and his co-workers,[6] Jackson,[7] McCrea and Meek,[8] Cohen,[9] Debré, Leroux and Hazard[10] and Johnston,[11] with results similar to those just described. The influence of the autonomic nervous system on the action of the mercurials was studied by Salant and Kleitman,[12] who showed that neither bilateral vagotomy nor atropinization would alter the effect, and by Salant and Brodman,[13] who found that epinephrine improved the heart poisoned with mercury while paralysis of the sympathetic nerve endings with ergotamine increased the toxicity of the mercurial. These results have been, in general, confirmed. It should be mentioned that there is no evidence from animal experiments that a sudden pooling of blood in the periphery is responsible for the effects of these drugs, as would be the case with an anaphylactoid reaction or the like.

The possible treatment of the cardiac irregularities following the mercurial diuretics is being considered and will be reported shortly. Johnston[11] showed that the isolated turtle heart recovered from mercurial poisoning by treatment with sodium thiosulfate. It has been found that this occurs also in the intact cat. The action of sodium formaldehyde sulfoxylate is being investigated in this connection.

CONCLUSIONS

1. The lethal doses for six mercurial diuretics when injected intravenously in the cat so as to kill within twenty to thirty minutes are salyrgan-theophylline 1.11, mercupurin 0.83, mercurin 0.70, salyrgan 0.41, esidrone

6. Salant, William, and Brodman, K.: J. Pharmacol. & Exper. Therap. **36**: 195 (June) 1929. Salant, William, and Nagler, H., ibid. **41**: 407 (April) 1931. Salant, William, and Nadler, J. E.: J. Lab. & Clin. Med. **13**: 117 (Nov.) 1927. Salant, William: Pharmacology of Mercury, J. A. M. A. **79**: 2071 (Dec. 16) 1922; Conditions Modifying the Action of Drugs, Tr. Sect. Pharmacol. & Therap., A. M. A., pp. 49-69, 1924. Salant and Kleitman.[12] Salant and Brodman.[13]

7. Jackson, D. E.: J. Pharmacol. & Exper. Therap. **29**: 471 (Oct.) 1926.

8. McCrea, F. D., and Meek, W. J.: J. Pharmacol. & Exper. Therap. **36**: 295 (July) 1929.

9. Cohen, S. J.: J. Pharmacol. & Exper. Therap. **35**: 343 (April) 1929.

10. Debré, R.; Leroux, H., and Hazard, R.: Compt. rend. Soc. de biol. **125**: 518, 1937.

11. Johnston, R. L.: J. Lab. & Clin. Med. **27**: 303 (Dec.) 1941.

12. Salant, William, and Kleitman, N.: J. Pharmacol. & Exper. Therap. **19**: 315 (May) 1922.

13. Salant, William, and Brodman, K.: J. Pharmacol. & Exper. Therap. **37**: 121 (Oct.) 1929.

0.24 and esidrone without theophylline 0.27. These values are in cubic centimeters per kilogram and have been adjusted to a mercury content of 40 mg. per cubic centimeter.

2. Previous treatment with oral ammonium chloride, oral phenobarbital, intravenous aminophylline and intravenous digitaline Nativelle had no effect on the lethal dose of mercupurin.

3. At least in the case of mercupurin, the lethal dose is smaller the slower the rate of injection (or the greater the interval between injections). This suggests (*a*) that the sudden death following these drugs cannot be avoided by slow injection and (*b*) that lethal doses of the various drugs should be compared only when the animals die within the same average time interval.

4. Dilution of the drug is of little value in preventing death from the intravenous injection of mercupurin.

5. Death is caused by action of these drugs on the heart. An early manifestation is a change in intraventricular conduction while the terminal effect is either ventricular fibrillation or respiratory failure secondary to the cardiac action.

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SUDDEN DEATH AND MERCURIAL DIURETICS

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Our purpose in this communication is to report the death of 4 patients following the injection of different mercurial diuretics and to point out the similarity of the cardiac function of these patients at the time of death to the experimental cardiac arrest in dogs produced by mercury.

Jackson [1] reported on the pharmacologic action of organic mercury compounds on the heart. By using 5 cc. of a 2 per cent solution of salyrgan intravenously, he was able regularly to produce death by ventricular fibrillation within three to five minutes in normal dogs under ether anesthesia. If the vagus inhibition of the heart was removed either by direct section or by large doses of atropine, death occurred from respiratory failure before the onset of ventricular fibrillation. He was of the opinion that the mercurials acted primarily on the heart through the mechanism of stimulation of the vagus and secondarily on the respiratory center if the vagal effect was removed. Salant and Kleitman [2] had previously observed ventricular fibrillation in normal dogs following the intravenous administration of inorganic mercurial salts and mercurochrome. Chastain and Mackie [3] studied the effects of esidrone (an organic mercurial with theophylline) on normal dogs anesthetized with barbiturates. They were regularly able to produce death by giving large intravenous doses of mercury salts. From twelve to fifteen seconds after the administration the electrocardiogram showed deviations of the T waves, followed by ventricular flutter and fibrillation. Death occurred in from three to five minutes.

Five deaths following the use of mercurial diuretics have been reported.[4] Each of the patients was suffering from the nephrotic type of renal disease and 4 of the 5 were children. Since each patient had received previous injections, "anaphylaxis" was considered the cause of death.

To the reported cases we wish to add the reports of the deaths of 4 adults with the following clinical and anatomic diagnoses: (1) coronary sclerosis, tabes dorsalis and minimal evidence of syphilitic heart disease; (2) nephrotic state of chronic glomerulonephritis; (3) hypertensive cardiovascular disease with decompensation, and (4) hypertensive cardiovascular disease with cirrhosis. In reporting these cases, only the significant clinical, laboratory and postmortem observations will be given.

CASE 1.—H. T., a white man aged 59, was seen Nov. 25, 1930 because of weakness and moderate dependent edema associated with arteriosclerotic heart disease and tabes dorsalis. The electrocardiogram showed a rate of 90, sinus mechanism, slurring of the QRS in all three leads and absent ST intervals. The blood pressure was 120 systolic and 80 diastolic. His general condition was greatly improved on a low sodium-high potassium diet together with 2 Gm. of ammonium nitrate after meals. There were occasional recurrences of edema and breathlessness which became more difficult to control, so that short periods of bed rest were required. Between 1932 and 1935 twelve intravenous injections of salyrgan were given, with excellent diuretic response. Even though the patient felt well most of this time, wasting of the body, characteristic of chronic cardiovascular disease, was indicated by a gradual loss of weight from 163¾ pounds (74 Kg.) in 1930 to 116 pounds (52.6 Kg.) in 1935.

On Jan. 15, 1935 2 cc. of mercupurin was given slowly intravenously and from three to five minutes later the patient sat up in bed, his eyes turned upward and he fell back unconscious. Twitching of the body, deep cyanosis and asystole were followed by an occasional ventricuar contraction, then short runs of what were interpreted as auricular fibrillation. The patient regained consciousness and a normal mechanism was resumed. It was estimated that the whole episode lasted about ten minutes, and the patient felt perfectly well in half an hour. His usual activity was resumed during the next few weeks. Edema gradually accumulated and on April 12 it was decided to administer a mercurial diuretic. Because of the previous episode, this time 2 cc. of salyrgan (plain) was administered slowly intravenously. Two minutes later a few extrasystoles were noted, there were rapid runs of fibrillation, the patient became very restless and then what seemed to be a ventricular tachycardia followed. The patient rose in bed, became deeply cyanosed, rolled his eyes and fell back dead. Asystole was followed by a fine rumbling sound over the precordium and was interpreted as ventricular fibrillation.

Autopsy showed an ancient occlusion at the orifice of the left circumflex artery and mild syphilitic change of the aorta but nothing could be found that might explain the sudden death.

Thus two different mercurial diuretics produced almost identical episodes in the same patient; the second ended fatally. This caused us to watch patients

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From the Department of Experimental Medicine, Northwestern University Medical School, and the Medical Ward of Passavant Memorial Hospital.

1. Jackson, D. E.: J. Pharmacol. & Exper. Therap. **29:** 471 (Oct.) 1926.

2. Salant, William, and Kleitman, Nathaniel: J. Pharmacol. & Exper. Therap. **19:** 315 (May) 1922.

3. Chastain, L. L., and Mackie, G. C.: South. Med. & Surg. **102:** 5 (Jan.) 1940.

4. Wolf, I. J., and Bongiorno, H. D.: Canad. M. A. J. **25:** 73-75 (July) 1931. Greenwald, H. M., and Jacobson, Seymour: J. Pediat. **11:** 540 (Oct.) 1937. Molnár, István: Klin. Wchnschr. **14:** 239 (Feb. 16) 1935. Tyson.[5]

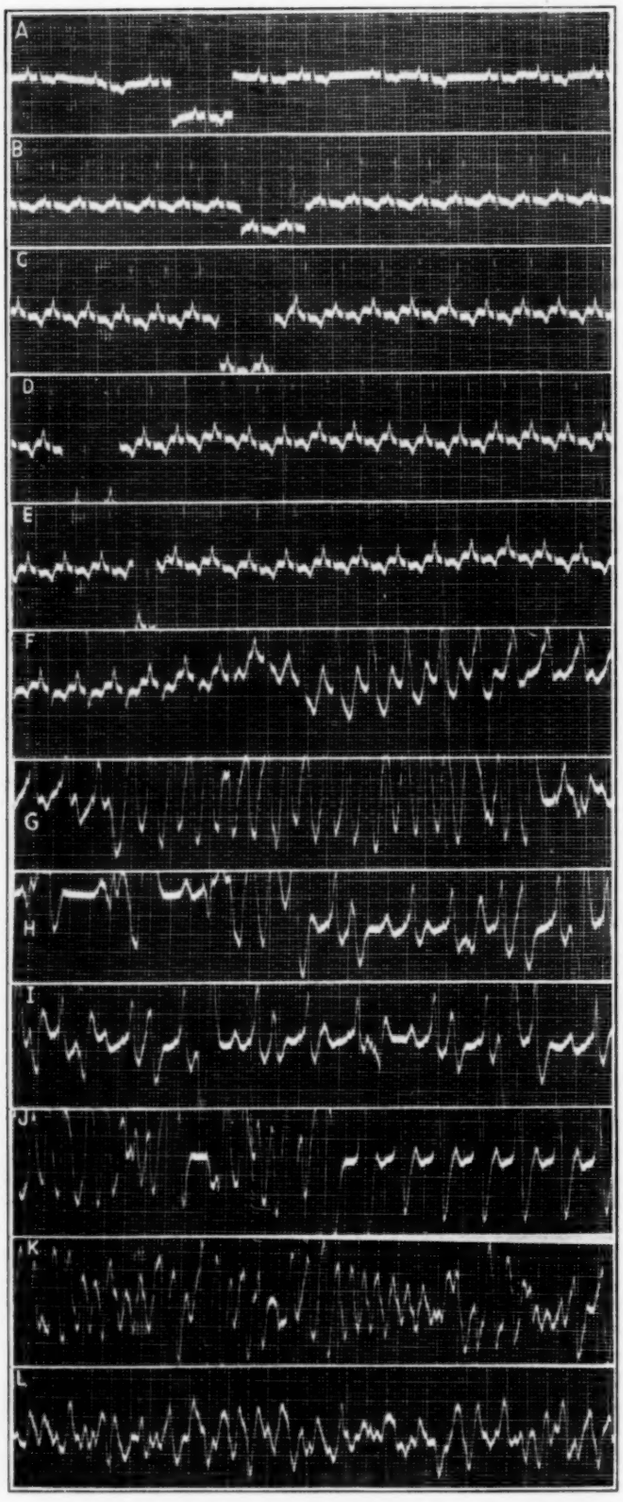

Fig. 1 (dog 150; weight 7 Kg.).—Intravenous soluble pentobarbital anesthesia was given; vagi were severed and 2 cc. of salyrgan was injected intravenously. *A*, control unanesthetized: sinus arrhythmia; inverted T waves; rate approximately 105. *B*, control anesthetized: QRS shows decreased amplitude; normal sinus mechanism with tachycardia; T waves inverted; rate 170. *C*, after the right vagus was cut: P waves increased; sharply inverted T waves; rate 160; increased amplitude of QRS. *D*, after the left vagus was cut: T waves sharply inverted; rate 164. *E*, during the injection of 2 cc. of salyrgan: rate 154. *F*, ten seconds after injection: ST segment depressed; changed to ventricular tachycardia. *G*, fifteen seconds after injection: continued ventricular tachycardia and fibrillation. *H*, thirty seconds after injection: ventricular tachycardia and extrasystoles. *I*, one minute after injection ventricular extrasystoles. *J*, three minutes after injection: ventricular fibrillation and extrasystoles. *K*, five minutes after injection: ventricular fibrillation. *L*, six minutes after injection: respirations ceased; ventricular fibrillation; tracing continued unchanged for five minutes.

more closely following the administration of these drugs, and three more deaths have been observed in the past six years.

CASE 2.—W. G., a man aged 48, entered the hospital with a history of generalized edema associated with a gain of 15 pounds (6.8 Kg.) in two months. Five months previously he had a severe infection of the upper respiratory tract with pharyngitis but otherwise had been in perfect health except for questionable scarlet fever in childhood. The patient had a pale, pasty appearance with definite edema of the face, hands, abdominal wall, sacrum and thighs. The blood pressure was 148 systolic and 90 diastolic. The tonsils were small and atrophic, with evidence of infection. The cervical lymph nodes were palpable. The urine contained 4 plus albumin, a few cellular and hyaline casts and doubly refractile lipoid bodies. The specific gravity was 1.022. Blood chemistry revealed a blood urea nitrogen of 15 mg. per hundred cubic centimeters, phosphorus 3.46 mg., cholesterol 625.0 mg. and total protein 3.1 Gm. per hundred cubic centimeters with inversion of the albumin-globulin ratio; the urea clearance was 50 per cent of normal; phenolsulfonphthalein excretion was 55 per cent in two hours. The basal metabolic rate was —15. Hemolytic streptococci were present in cultures of material taken from the throat.

The clinical diagnosis was chronic glomerulonephritis in the nephrotic stage. He was placed on a salt free, high protein diet with 2 Gm. of ammonium chloride after meals, but after six weeks there was little improvement. The removal of his infected tonsils was followed by an acute exacerbation of the glomerulonephritis. During the next four months the disease progressed, as indicated by a decreased kidney function, a rise in blood pressure and an increase in the anemia and edema. During this period blood transfusions, hypertonic solutions and acacia failed to modify the persistent edema. The most helpful regimen had been a low sodium, low phosphorus diet with 2 Gm. of ammonium nitrate after meals and potassium chloride as a salt substitute. Finally, six months after his admission, it was decided to attempt a diuresis with the aid of a mercurial diuretic. On the morning this was given the patient was comfortable and ambulatory. Blood pressure was 170 systolic and 100 diastolic, and the pulse was 80 and regular. Two cc. of mercupurin was given slowly intravenously (diluted to 10 cc. in isotonic solution of sodium chloride). Within five minutes after the administration of the drug the patient, who had been lying quietly in bed, suddenly gasped, stiffened and then relaxed. A period of forceful irregularity of the heart was noted, followed by a decrease and finally absence of any sounds. The patient failed to respond to artificial respiration or intracardiac administration of epinephrine.

This patient in a nephrotic stage of chronic glomerulonephritis, after several months in the hospital on a low sodium, low phosphorus diet, died following the initial injection of 2 cc. of mercupurin. The sequence of events was injection followed in three to five minutes by a gasp, stiffening, relaxation with an associated cardiac irregularity, then death.

The postmortem diagnosis was subacute glomerulonephritis with parenchymatous fatty degeneration associated with generalized edema, hydrothorax, hydropericardium and ascites. No cause was found for this sudden death. During fifteen years of the use of mercurial diuretics in nephritic disorders [5] this is the only death that could be attributed to the drug.

CASE 3.—Mrs. M. D., aged 64, was admitted to the hospital for the fifth time in two years with a diagnosis of hypertensive cardiovascular disease with cardiac decompensation. For two years prior to her first hospital admission she had been bedridden. During this time her family physician had given her ammonium chloride and salyrgan at ten to fourteen day intervals

5. Tyson, Mary Catherine: Danger of Intravenous Mercurial Injection in Nephrosis, J. A. M. A. **117**: 998 (Sept. 20) 1941.

to control the edema. Subsequent to her first hospitalization she became edema free and remained fairly well controlled on an acid ash, low sodium diet with added ammonium and potassium salts. Occasional bouts of hypertensive encephalopathy and cardiac decompensation necessitated hospitalization.

At the time of her final admission she complained of fatigue, epigastric distress and orthopnea. Physical examination revealed fluid in the right side of the chest, an enlarged liver and ascites. The blood pressure was 200 systolic and 115 diastolic. The heart was enlarged to the left and there was a gallop rhythm. The urine contained 2 to 3 plus albumin with rare red blood cells and hyaline casts. The red blood cell count was 3.03 million and the hemoglobin 9 Gm. During the four months of her hospital stay there was a slight progressive diminution of renal function and the cardiac status became worse. The edema became more difficult to control despite digitalis and various diuretic salts (ammonium nitrate and chloride and potassium nitrate and chloride). During this period four intravenous injections of salyrgan and theophylline (2 cc. in 10 cc. of isotonic solution of sodium chloride) were given without notable diuresis. During the next twenty-eight days diuretic minerals and digitalis were discontinued. One mg. of urginin was given three times a day, since it was believed that digitalis had produced nausea. Finally it was decided to try a mercurial diuretic again, and twenty-eight days after the last injection 4 cc. of salyrgan and theophylline was given intravenously. Two minutes later she gasped and became cyanotic, and a rapid irregularity of the heart promptly developed. After a few irregular forceful ventricular beats there was cardiac standstill, and death occurred within three minutes of the injection.

The salient features of the postmortem examination were generalized arteriosclerosis, diffuse fibrosis and hypertrophy of the heart, with an old infarct in the intraventricular septum and advanced arteriosclerosis of the kidneys. The general picture was that of chronic passive congestion of the viscera and free fluid in the serosal cavities. Microscopic examination of the tissues failed to reveal any cause for the sudden death.

It is estimated that during the five year period this patient had received more than two hundred injections of mercurial diuretics. At the time of her death, her true weight was approximately 75 pounds (34 Kg.). It is conceivable that the patient received a toxic dose in view of her reduced body weight or because of the severe degree of cardiac damage.

CASE 4.—Mrs. Z. T., aged 64, with a history of diabetes, entered the hospital in a somnolent condition. There was a history of increasing edema of six months' duration. The diabetes had been controlled by 65 units of protamine zinc insulin daily. The patient had received fifteen injections of mercurial diuretics, but none had been given six months prior to admission to the hospital. On admission she was massively edematous and dyspneic, with a history of relative anuria of less than 500 cc. daily. The blood pressure was 160 systolic and 116 diastolic; the heart was enlarged to the left and the pulse was regular at 100 beats a minute. Examination of the urine was negative for sugar and acetone, but it contained 4 plus albumin. Blood sugar was normal.

It was deemed advisable to add 1 cc. of salyrgan through a gravity drip rather than give it directly, in the hope that this slow injection would produce no ill effect. After thirty minutes, while the solution was still running, the patient, who had apparently been relatively comfortable, suddenly gasped for breath, became cyanotic and vomited. A coarse irregular heart action was heard, the pulse became imperceptible and respirations ceased. Death occurred twenty-two hours after admission.

The autopsy showed arteriosclerosis of the kidneys, cardiac hypertrophy and dilatation, and pulmonary atelectasis.

This patient was moribund on admission, and death might have occurred without any medication, but it seems that it is more than a mere coincidence that death should occur in this manner during the time of injection of the mercurial diuretic.

In view of these clinical experiences it was decided to study the effect of the various mercury salts experimentally on the heart by the electrocardiogram and by direct observation. Mercurial compounds injected intravenously into 30 normal dogs produced death by a particular pattern, namely depression of the T waves, runs of extrasystoles, ventricular tachycardia, ventricular fibrillation and death. In animals under intravenous barbital anesthesia the mechanism was the same. Similar results were obtained when 4 animals were vagotonized, and in 2 animals when the cervical cord

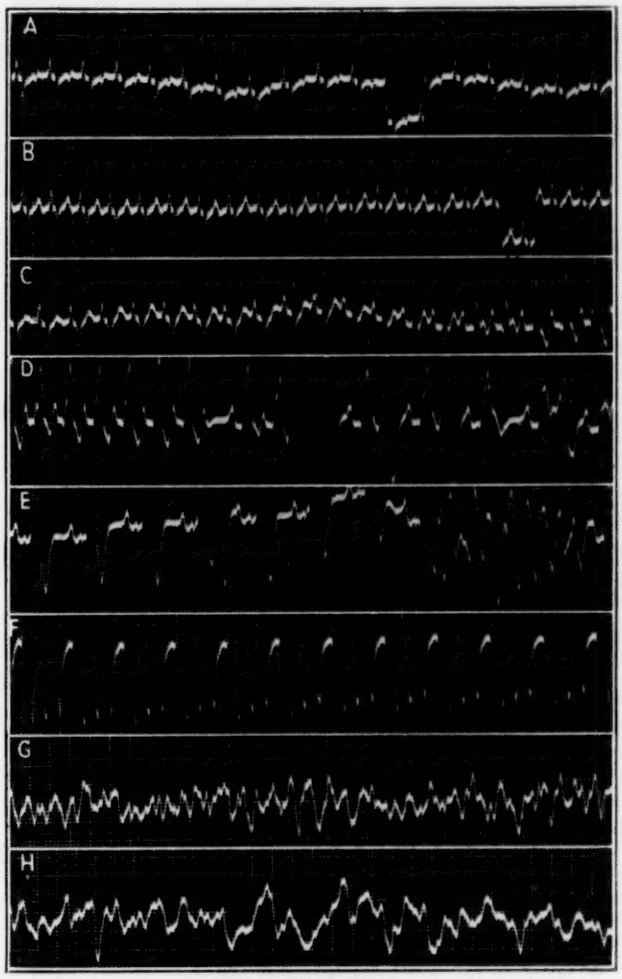

Fig. 2 (dog 50; weight 8 Kg.).—Intravenous soluble pentobarbital anesthesia was given; the spinal cord was severed at the lower cervical region and 2.2 cc. of salyrgan and theophylline was given intravenously. *A*, control before the cord was severed: inverted T waves; rate 17. *B*, control after the cord was severed: T waves upright; rate 190. *C*, fifteen seconds after the injection: ST interval depressed and slurred; rate 190; beginning ventricular extrasystoles. *D*, twenty seconds after the injection: ventricular extrasystoles. *E*, thirty seconds after injection: ventricular extrasystoles changing to ventricuar fibrillation. *F*, one minute after injection: ventricular extrasystoles. *G*, four minutes after injection: respirations ceased; ventricular fibrillation. *H*, eight minutes after injection: the tracing showed ventricular fibrillation after four more minutes; the only change was decrease in amplitude.

as well as the vagi were severed, and in instances of an isolated perfused heart. It was noted that the sequence of events was almost identical in a large number of instances, and after cessation of all ventricular electrical impulses, as observed by the electrocardiogram, the auricles continued with a regular sinus

rhythm. The observations were made with equivalent amounts of either organic or inorganic mercurial compounds. From these studies it is our impression that the mercury ion acts directly on the ventricular muscle to produce ventricular fibrillation and death. Complete studies are being published elsewhere.

COMMENT

In a search for common factors and pertinent points in these four deaths following mercurial diuretics we note that all 4 patients had suffered from some chronic wasting disease. Edema had been present in variable amounts over many months. Each patient had received diuretic salts, chiefly ammonium nitrate and potassium chloride, in variable amounts as a salt substitute. The sequence of events leading to death were similar. Three patients who had had definite cardiac damage received digitalis occasionally, but none were taking it at the time of death. However, 1 patient was taking urginin. Two patients had advanced renal disease and a third had moderate cirrhosis of the liver. Three of the patients had received numerous injections of different mercurial diuretics (ranging from fifteen to two hundred) while the nephrotic patient died following the initial dose. To date we are unable to correlate the method of administration of the drugs, adjunct mineral diuretic salts or changes in the body chemistry with these fatalities. Because of the wasting of the body tissue, which is striking in the edematous patient, we were unable to exclude a toxic effect of a relative overdose of mercury. Whether in patients or in dogs, death by cardiac arrest is similar regardless of the type of mercurial compound employed.

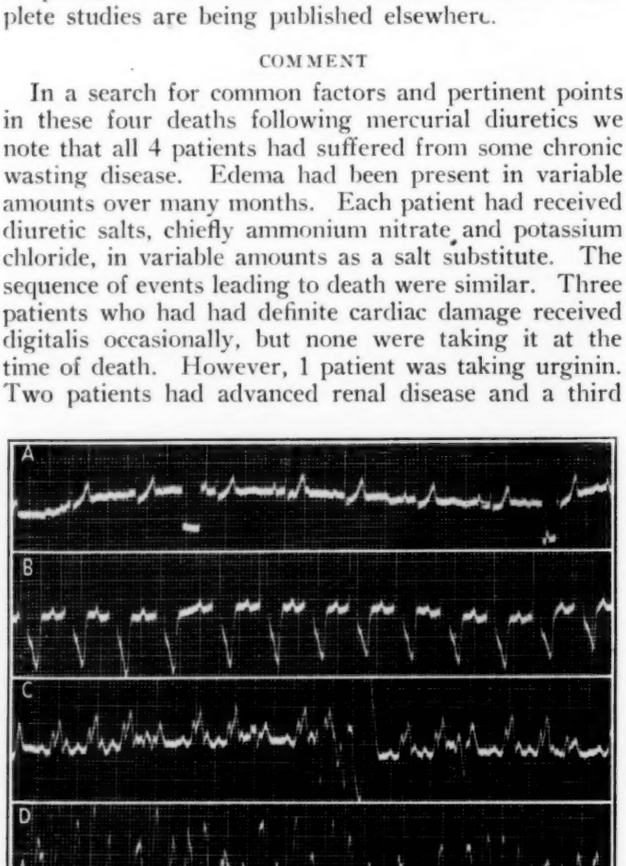

Fig. 3 (dog 960; weight 7 Kg.).—No anesthesia; 1.4 cc. of mercupurin injected intravenously. *A*, control on Sept. 3, 1941. *B*, twenty seconds after injection. *C*, one minute after injection. *D*, two minutes after injection. *E*, three minutes after injection: respiration ceased at this time; the same type of tracing continued for two minutes, at the end of which time the electrocardiograph was stopped.

It is far from the intent of this report to deter from the clinical use of mercurial diuretics but rather to emphasize caution in their intravenous use in the waterlogged, wasted patient.

DEATHS IMMEDIATELY FOLLOWING THE INTRAVENOUS ADMINISTRATION OF MERCUPURIN

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The fact that there are but few reports of serious accidents following the intravenous administration of mercupurin gives the impression that such reactions are very infrequent. Tyson [1] reported two deaths following the intravenous administration of mercurial diuretics (esidrone and mercupurin) to patients with nephrosis. She also cites other deaths in the literature from other mercurial diuretics. But we know of no reports of deaths following the use of mercupurin in patients with congestive heart failure.

Each of us has given a large number of injections of mercurial diuretics during the past six or seven years to patients with congestive heart failure; our combined experience exceeds many thousands of injections, yet none of us had previously seen a serious or fatal reaction. It was with great surprise, therefore, that we learned that within a short space of time we had independently observed deaths immediately following the administration of mercupurin. A short letter to the editor concerning three of these deaths was printed in an earlier issue of THE JOURNAL.[2] Since then we have heard of other deaths and we are able to add the fourth case (case 1).

As far as we can judge, the technic of injection in each instance was satisfactory. The injections were made slowly, although not actually timed. Needles of small caliber (23 to 26 gage) were used. Blood was withdrawn into the syringe and mixed with the mercupurin. Since ampules of mercupurin are not "lot marked," it has not been possible to determine whether any one particular lot was responsible for all the reactions. Unfortunately, postmortem examinations could not be performed.

CASE 1 (Dr. Brown).—A man aged 68 with a history of angina of effort for about ten months and acute myocardial infarction for four months before his death had, during the first days following the myocardial infarction, repeated attacks of left ventricular failure. For the relief of this he had received ammonium chloride and aminophylline without benefit.

On the fourth day of the illness he was given 1 cc. of mercupurin intravenously. Before the needle could be withdrawn the patient became unconscious, respirations became shallow and the face became very pale. The pulse rate fell to 20 or 30 beats a minute. Within thirty seconds there was a spontaneous recovery, but within the next five minutes this type of syncopal seizure was repeated four times. In the interval between seizures the pulse rate was rapid and became very slow during an attack. There was full spontaneous recovery after this. An electrocardiogram did not give evidence of heart block, which was presumed to have occurred during the seizure.

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1. Tyson, Mary Catherine: Danger of Intravenous Mercurial Injections in Nephrosis, J. A. M. A. **117:** 998-999 (Sept. 20) 1941.

2. Friedfeld, Louis; Kissin, Milton; Modell, Walter, and Sussman, R. N.: Mercupurin, correspondence, J. A. M. A. **117:** 1806 (Nov. 22) 1941.

About five days later, because of increasing hepatomegaly and dyspnea, an injection of mercupurin was prescribed. By error it was given intravenously instead of intramuscularly as ordered. This time there was but a single seizure like that already described, lasting about one minute, with prompt recovery.

On subsequent examination it was determined that a large ventricular aneurysm had developed. In the ensuing four months there were repeated attacks of paroxysmal dyspnea and pulmonary edema. Mercupurin was given ten times intramuscularly with good diuretic effect and no reactions. During the last episode of pulmonary edema, after morphine and oxygen had been given without benefit, the physician in charge did not observe the injunction against intravenously administered mercupurin and gave 2 cc. of mercupurin intravenously. Within one minute the patient was dead. The pulse and the exact behavior of the patient during this episode were not recorded.

CASE 2 (Drs. Friedfeld and Kissin).—A housewife aged 52 with a twelve year history of diabetes and a four year history of hypertension had about a year before the final episode suffered an attack of constrictive pain in the chest on walking. An electrocardiogram showed the changes of ventricular strain on the left side seen in hypertension of long duration. About a month after this there was a sudden severe attack of viselike pain in the chest with the typical picture of acute myocardial infarction, although this was not corroborated by the electrocardiogram. Two months later she suffered a pulmonary infarction.

About four months before death the patient was seen in congestive failure: the liver was enlarged and ascites, rales in the chest, dyspnea and orthopnea were present. Digitalis was given (1 cat unit daily). Ammonium chloride and mercupurin suppositories were followed by good diuretic effect. Five-tenths cc. of mercupurin given intramuscularly was effective and at five day intervals other mercupurin injections were given intramuscularly, until one of them was followed by slough. After this the patient refused to submit to intramuscular injections, so that all subsequent injections were given intravenously.

About one month later 1 cc. of mercupurin was given intravenously. From one to two minutes after the completion of the injection severe dyspnea and orthopnea developed. The cardiac rhythm was unchanged and the pulse was of good quality. The episode lasted from two to three minutes.

Despite exceedingly slow injections similar attacks followed seventeen of eighteen subsequent injections, but since the patient steadily refused any but intravenous injections this mode of administration was continued. The dose of mercupurin was gradually increased to 2 cc.

The last injection was 2 cc. In less than one minute the usual dyspnea and orthopnea developed. It subsided and the patient started to chat with her daughter. Suddenly, about three minutes after the completion of the injection, her face flushed intensely and she collapsed. A pulse was not palpable and no heart sounds were heard. After a few gasps the patient was dead.

CASE 3 (Dr. Modell).—A woman aged 48 with syphilitic heart disease and aortic insufficiency of many years' duration suffered from congestive heart failure. After digitalis (2 cat units daily) no longer prevented decompensation and her liver became larger and edema appeared in her legs and lungs she was given ammonium chloride and weekly doses of 2 cc. of mercupurin intravenously. During the forty-two weeks preceding her death she had received as many weekly injections with no untoward effect. Each injection was followed by a gratifying diuresis, so that the patient would look forward to her treatment, as fluid accumulated during the week.

The last injection was given in the same manner as all the prior injections had been, with the patient sitting. On completion the patient appeared normal. About two minutes later, while the patient was resting with her arm crooked to compress the injected vessel, she tapped her physician on the shoulder to bring his attention to her. Apparently unable to speak, she pointed to her chest, presumably indicating some type of substernal distress. Then she fell forward. She was placed supine on the floor. There was no respiration, no pulse; heart sounds were not heard; cyanosis developed rapidly.

Artificial respiration with cardiac massage was attempted for a few minutes without effect. One cc. of epinephrine (1:1,000) was injected into the heart without effect. Artificial respiration was resumed for about fifteen minutes without avail.

CASE 4 (Dr. Sussman).—A woman aged 60 with a history of hypertension and myocardial infarction of three years' duration and congestive failure for the past two years had during the last year and a half been receiving digitalis and various diuretic drugs. The electrocardiograms indicated myocardial damage and infarction of the anterior and posterior wall. During her stay at a hospital in the early stages of her illness the record states that she received mercurial diuretics intravenously with "unpleasant effects." The patient later repeated to her physician that "unpleasant effects" immediately followed these injections. Striking symptoms in this patient were the coldness and pallor of her limbs and face, with intermittent generalized sweating.

When she was discharged from the hospital there was enlargement of the liver. Oliguria was severe except after the administration of mercupurin. During the one month preceding her death she received digitalis (1 cat unit daily), ammonium chloride and weekly injections of mercupurin. Salt and fluid intake were restricted. Her blood pressure for the two weeks preceding her death was low as compared with previous determinations.

Four injections of mercupurin were given to the patient at her home without reaction. The last injection (2 cc.) was given by the same technic. Immediately after its completion the patient's face flushed intensely. She made an effort to speak but could not. Her heart rate slowed to about 30 beats a minute. The intensity of heart sounds varied. Cyanosis quickly became more intense. Death occurred within four minutes of the completion of the injection.

COMMENT

It is noteworthy that in 3 of the 4 cases presented there was a history of previous reactions following the intravenous administration of mercupurin. In 2 cases a change in cardiac rhythm was observed, on 2 occasions in 1 case.

That the reaction was not due to the theophylline component in 1 case is borne out by the fact that seven times the dose present in 1 cc. of mercupurin was given without ill effect (case 1).

Whereas 3 of these patients had received intramuscular injections of mercupurin on numerous occasions without reactions, the intravenous administration was the method used in all the fatal instances. It is also significant that in all the fatal injections the dose was 2 cc.

All the patients were known to have adequate renal function as judged by the specific gravity of the urine. It is also worth noting that in all cases previous injections of mercurials had been followed by generally satisfactory diuresis.

SUMMARY

In cases of congestive heart failure the intravenous injection of 2 cc. of mercupurin was followed by immediate death.

In 3 of the 4 cases immediate reactions were noted after intravenous injections prior to the final one. These included dyspnea, orthopnea, sweating, pallor, bradycardia and syncope. In no case was there a delayed reaction such as might be due to massive diuresis, loss of chloride or disturbance of the electrolyte balance. In all the patients a satisfactory but not massive diuresis followed previous injections of mercupurin.

Two of the 4 patients had received intramuscular injections with adequate effect and without toxic reactions on previous occasions.

A REVIEW OF THE TOXIC MANIFESTATIONS OF MERCURIAL DIURETICS IN MAN

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Recent publicity [1] given to sudden deaths which were believed to have resulted from the use of mercurial diuretics prompted us to review the entire subject of the acute toxicity of these drugs. In this issue of THE JOURNAL DeGraff and Lehman [2] have reported the results of experiments on cats to determine the possible mechanisms involved. This report will deal with the various untoward reactions that have been observed in patients. Toxic manifestations other than those of purely local nature, e. g. at the site of injection, may be roughly divided into two major groups: (1) those not directly related to the diuretic but to the associated diuresis and (2) those directly related to the drug.

First we shall consider the toxic reactions not related to the drug. As early as 1891, Jendrässick [3] in giving mild mercurous chloride to patients with cardiac edema noted an increase in the urinary excretion of water and chlorides. Saxl and Heilig,[4] who were the first to discover that merbaphen (novasurol) caused a strong diuretic response in patients with cardiac edema, also demonstrated not only a relative but also an absolute increase in the chlorides excreted in the urine. These facts have been amply corroborated.[5] Coincident with the diuresis there is a decrease in the blood serum chlorides.[6] This fall in the serum chlorides is due to the fact that the amount of chloride found in the extra urine excreted is greater than that of an equivalent volume of body fluid.[7] Blumgart and his associates [8] found that the fall in serum chloride is secondary to the diuretic effect of the mercurial on the kidney and is not essential for the production of diuresis. Furthermore, Evans [9] observed that the response to mercurials depends on the available supply of chloride and water in the tissues.

Symptoms of chloride depletion may be produced, therefore, as a result of mercurial diuresis. This picture is seen also in other instances of excessive chloride loss, such as in heat prostration and in pernicious vomiting. Thus one may get a syndrome characterized by profound weakness, apathy, somnolence, disorientation, delirium and occasionally coma.[10] Muscle pains, especially in the calf muscles, are frequently prominent. McCance and Widdowson [11] noted mental symptoms in all cases of experimentally induced salt depletion with dehydration. Poll and Stern [10] reported 7 cases of dehydration following the use of mercurial diuretics in patients with heart failure, and they too were impressed by the mental symptoms, especially the preliminary ones of restlessness and confusion. In the more severe states of dehydration, psychoses sometimes progressing to coma and death may result.[10]

The serum sodium and calcium usually do not change appreciably after mercurial diuresis even though the diuresis may be considerable.[12] Nothmann[13] observed a lowering of serum calcium in a few cases, but in others no change was noted. Spontaneous tetany [13] developed in some instances but was not necessarily associated with a drop in the serum calcium level. Tetany after repeated injections of mercurial diuretics was also noted by Pavel and his associates.[14] Grand mal attacks are said to have been provoked in epileptic patients by mercurial diuresis.[15]

It is quite possible for edema to be still present even though there are dehydration, a negative chloride balance, and hemoconcentration as a result of mercurial diuresis.[16] Thus oliguria or anuria may result from a deficiency of salt to aid in the excretion of water. Unless the mechanism is properly understood in such cases, the dose of the mercurial may be increased or the interval between doses decreased. Then, added to the factor of dehydration may be that of mercury poisoning due to poor excretion of the drug. Hines [17] and Evans and Paxon [18] concluded that azotemia after the use of mercurial diuretics is more likely the result of the rapid removal of large amounts of edmatous fluid than the result of damage to the kidney from mercury.

Price [19] reported the development of gout following salyrgan [20] diuresis in 5 patients who had a previous history of gout. He stated that it was not due to mere mechanical concentration of uric acid in the tissues as a result of the diuresis. We observed a patient in congestive heart failure who had a history of gout but were unable to precipitate an attack of gout with repeated profuse diuresis by mercupurin,[21] even though an attack could readily be induced by a high purine diet.

It is evident from the foregoing that, unless the electrolyte and water balance are carefully controlled, symptoms of considerable severity are possible merely as the result of rapid diuresis and not primarily owing to a toxic reaction following the use of a mercurial diuretic. Care must therefore be taken to keep the patient in salt balance. Symptoms such as muscle cramps are usually prevented by the administration of ammonium chloride to replace the chloride lost by diuresis.

Another important toxic manifestation related not directly to the mercurial but rather to the rapid diuresis is digitalis toxicity due to a mobilization of digitalis

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21. The names mercupurin, novurit and mercurophylline, U. S. P. XII, are essentially synonymous.

from retained tissue fluids when a fully digitalized patient is given a mercurial diuretic. Miller and Smith [22] found that edema fluids of digitalized patients when tested on the cat contained an appreciable amount of a digitalis-like substance, whereas fluids from controlled undigitalized patients produced no effect. The same effect was later demonstrated by Schnitker and Levine [23] on the Straub heart preparation in the frog. They showed, as did Gouley and Soloff,[24] Kissane and Koons [25] and Hyman,[26] that redigitalization even to the point of toxicity could be produced as these body fluids found their way back to the blood stream and out through the kidney during a mercurial diuresis. Rapid diuresis in fully digitalized patients may bring on typical signs and symptoms of digitalis toxicity not present prior to the administration of the mercurial diuretic. Our experience is in accord with that of the investigators cited. Symptoms of digitalis toxicity may develop with the loss of considerable edema fluid even though digitalis has not been administered for several days. It is necessary, therefore, that considerable caution be exercised in the administration of a mercurial diuretic to a patient who has been fully digitalized. If the diuretic must be given, a small dose, i. e. 0.5 cc., should be used, preferably by the intramuscular route. If appreciable diuresis does not result, larger doses can then be given later.

In common with other potent drugs, cases of individual susceptibility or idiosyncrasy have been noted with the mercurial diuretics. All of the commercially available drugs of this group have at some time or other been reported as producing, in isolated instances, alarming symptoms and even death. In some cases this appears to be a susceptibility to mercury and is noted regardless of the preparation used.[27] In others the reactions seem to be related to the organic structure of the particular diuretic, because another preparation can subsequently be given with impunity (to be discussed later).

Those reactions which seem most clearly related to the mercury itself are the gastrointestinal and the renal disturbances. The effects on the gastrointestinal tract are typically those of mercury poisoning, namely stomatitis, salivation and hemorrhagic colitis. Merbaphen, one of the first of the mercurial diuretics, was the most frequent offender in this regard.[28] The development of stomatitis [29] and excess salivation [30] is not a particularly reliable early sign of mercurial toxicity, for, as Stokes [31] has pointed out, the presence of stomatitis is dependent as much on the bacterial flora of the mouth and incidental conditions as it is on the dose of mercury that the patient is receiving.

With the use of theophylline-containing mercurial compounds, the danger of mercurial poisoning may be considerably lessened because of the more rapid and complete excretion of the drug.[32]

The changes produced in the kidney by mercurial diuretics consist chiefly in degeneration of the epithelium of the tubules. As a rule, the signs in the urine of renal irritation which occur with use of mercurial diuretics appear in the following order: (1) casts, hyaline and granular, (2) albumin, (3) leukocytes, (4) erythrocytes. Sprague and Graybiel [33] and Herrmann and Decherd [34] have reported mild renal irritation produced by salyrgan, and Herrmann and Decherd [34] and Klinghoffer [16] have noted the same for mercupurin. Brown and Englebach [35] made counts of the urinary casts before and after the administration of clinical diuretic doses of salyrgan to 5 patients with ascites who had no evidence of renal disease. In every instance they found that the count was appreciably increased after the drug was given but that this effect was transient. Hematuria has been noted following the use of merbaphen [36] and salyrgan.[37]

A case of relatively severe renal irritation caused by salyrgan was reported by Derow.[38] In a series of necropsies on 30 patients who received salyrgan during life, Tarr and Jacobson [30] found only 1 patient with a renal lesion suggestive of mercurial intoxication. The risk of uremia as a complication is not great. Hines,[17] Evans and Paxon [18] and Klinghoffer [16] have shown that a rise in blood urea may occur. However, this is generally interpreted as due to rapid removal of edematous fluid with hemoconcentration rather than to kidney damage from the mercurial used.

While toxic anuria has been produced in animals by salyrgan [39] and 2 cases of anuria in man with extensive tubular damage found at necropsy were reported by Schwab and his associates,[40] it appears that extrarenal factors, such as disturbance of the electrolyte balance, are the more likely cause of anuria when present. Parent [41] observed a man aged 64 with coronary arteriosclerosis and previous myocardial infarction who had severe congestive heart failure. Digitalis was no longer effective, so 2 cc. of mercupurin was given intravenously. Anuria resulted and the patient died forty-eight hours later in coma with convulsions. Petersen [42] reported that 1 patient with anuria was given salyrgan, and not only was urinary flow reestablished but a satisfactory diuresis was obtained. Apparent anuria may be due to prostatic swelling following the diuresis, as was noted by Tscherning [43] with salyrgan in 4 old men with hypertrophied prostates.

Patients with evidence of kidney damage usually tolerate mercurial diuretics fairly well. However, as will be noted later, it is this group that furnishes us with a large proportion of deaths following the use

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of mercurial diuretics. The presence of kidney disease is a contraindication to the use of mercurial diuretics even though many times serious complications may not result.

Mercurial diuretics in common with other compounds containing mercury may on occasion produce cutaneous eruptions.[44] There is a striking variability in the type of reaction produced. Those particularly mentioned in the literature are urticaria,[45] small reddish spots or purpuric areas [46] and morbilliform [47] or scarlatiniform erythema.[48] Occasionally the rash is followed by desquamation in from one to three weeks. Patch tests by Wilson [49] demonstrated that these reactions may be on an allergic basis. In contrast, there may occur in rare instances a severe mercurial dermatitis due to an accumulation of mercury in the body. While the latter reaction was occasionally seen with the older type of mercurial diuretic, it is no longer observed with the rapidly excreted theophylline-containing mercurials.

An erythematous eruption may follow either the first or any subsequent injection of the diuretic. As a possible mechanism, Lesser [50] suggested that the mercury circulating in the blood stream caused paralysis of the sympathetic nerves with consequent vasodilatation. That capillary dilatation is also an effect of mercury on the skin is supported by the histologic studies of Almkvist.[51]

In those persons in whom sensitivity to a mercurial diuretic manifests itself by a rash, changing the route of administration from intravenous to intramuscular or rectal routes is of no avail.[27] While not serious in itself, the occurrence of a rash may be a warning of more serious reactions if one persists in the use of the mercurial. In the case reported by Wolf and Bongiorno,[47] a blotchy rash resembling measles was seen on the face following the fourth injection of salyrgan. The next injection, one week later, caused death within one minute.

Chills and fever have been noted with merbaphen,[52] salyrgan [53] and mercupurin.[54] Coventry [55] noted an elevation of temperature with mercupurin, and Robinson [54] had 1 patient who had a rise in temperature after each injection of mercupurin. The reaction is probably not due to pyrogenic material in the ampule because, in the first place, the maximum volume of fluid injected is 2 cc., and, in the second place, material from the same lot number caused no pyrogenic response in other patients. In some instances at least it would appear that individual susceptibility to a particular preparation is responsible, because changing to another mercurial produced no further reactions. Gold [56] had a patient who had a rise of temperature after the use of mercupurin but failed to get a reaction on changing to salyrgan with theophylline. We had the opportunity to observe a similar situation in a patient aged 68 with arteriosclerotic and hypertensive heart disease and severe congestive heart failure who received 2 cc. of mercupurin intravenously at weekly intervals. More than sixty injections had been given without any untoward effects. About one hour after the next injection rigor and a slight elevation in temperature developed. One week later an injection was followed by a more severe, prolonged rigor with a slight fever. The next dose of mercupurin was given intramuscularly and for the third consecutive week the patient had a chill, this time even more severe than before, and the temperature rose to 102 F. In each instance the temperature was normal the next day and an excellent diuretic response was obtained. Other patients receiving mercupurin from the same batch had no reactions. The next week and subsequently salyrgan with theophylline was given intramuscularly with good diuretic response and no chills or fever.

Reactions resembling a state of shock with chills, sweating, cyanosis, collapse and urinary suppression have occasionally been noted following the use of mercurial diuretics, namely merbaphen,[57] salyrgan,[53] mercupurin [58] and esidrone.[59] While it is generally considered that this syndrome is a direct result of mercurial poisoning, Poll and Stern [10] compare it to the similar clinical picture seen in Addison's disease and believe it to be due to loss of water and chlorides. It should be noted, however, that in many cases the acute reaction is observed long before the onset of diuresis. Another case reported to us by Parent [41] would indicate that here again individual susceptibility to a particular mercurial may be the important factor. His patient was an elderly man who had an old myocardial infarction and general anasarca and who had received several doses of mercupurin intravenously. Because the effect was much less than had been experienced previously, Parent decided to change to esidrone. Immediately after the administration of esidrone (no mercurial had been given for two weeks) the patient began to cough, his breathing became asthmatic, cyanosis appeared, followed by clonic convulsions of the hands and face, and he became unconscious with involuntary urination and defecation. Two minutes later the twitchings ceased, he regained consciousness, but coughing and heavy breathing continued for the next ten minutes. Subsequently mercupurin was again given without any reaction.

The first deaths reported were by Redlich [60] in 1925 from the use of merbaphen. There were three fatalities. In 1 case death occurred after two doses with a three day interval between; in another, a single dose of 1 cc. of merbaphen was followed three weeks later by death, which appeared to be due to enteritis and volvulus.

The next fatality was reported by Wolf and Bongiorno [47] following the use of salyrgan. Their patient was a 4 year old child with nephrosis who was given salyrgan intravenously in gradually increasing doses, up to 1 cc., about a week apart. The fourth injection, of 1 cc., was followed by a chill in about one hour and a rise in temperature to 102 F. The next morning the temperature was normal, a blotchy rash resembling measles was seen on the face and this was gone in

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two days. Within a minute after the fifth injection the child coughed, cried and fell dead.

Sundaram [61] reported the death of a boy aged 10 years with rheumatic heart disease who died after receiving his first dose of 0.5 cc. of salyrgan. The drug was diluted with 10 cc. of water and injected intravenously; in about five minutes the patient complained of a sudden pain in the chest, collapsed and died. Hug [62] reported a similar fatality in a case of severe myodegeneration and cirrhosis of the liver but believed that poor liver function contributed to the death. Cadbury [53] had 2 patients with nephritis who died following the use of salyrgan. One, a girl aged 21 with nephritis, was given salyrgan on three occasions; after the last injection of 2 cc. intravenously she became dizzy and was dead in five minutes. The other was a 5 year old boy with nephritis; 0.6 cc. of salyrgan was injected into the jugular vein; he collapsed and died in ten minutes in spite of epinephrine given intramuscularly and intracardially. Two other deaths have been reported by Barker and his associates.[63]

Sudden death due to neptal [64] was reported in 2 cases by Greenwald and Jacobson.[47] Their first patient was a child aged 2 years with nephrosis who was given 0.5 cc. of neptal intramuscularly followed by 1 cc. intramuscularly four days later. One week later 1 cc. of neptal given intravenously caused dyspnea, cyanosis, cardiac standstill and death within one minute of injection. The second patient was a child aged 3 years with nephrosis who received 0.5 cc. of neptal intravenously followed by 0.5 cc. given intravenously six days later. Three days later an injection of 0.5 cc. intravenously caused a convulsion, dyspnea, cyanosis and coma within two minutes and death in less than five minutes after the injection. They believe that death was due to anaphylactic shock.

The first two fatalities following the use of mercupurin were reported by Engel and Epstein.[65] In the first patient 1 cc. was given for edema of cardiac origin and a good diuresis was obtained, but two days after the injection an intractable bloody diarrhea developed. Examination of the feces proved negative and the patient died two weeks later. Postmortem examination revealed severe colitis. Though they could not identify the cause of the severe colitis, they did not consider that it could have been caused by a single injection of mercupurin. Their second fatality occurred in a case of bronchial asthma and decompensated arteriosclerotic heart disease. They gave 2 cc. of mercupurin intravenously and the patient died suddenly a few minutes after the injection. Postmortem examination revealed high grade narrowing of the lumens of the coronary arteries and extensive myocardial degeneration—a pathologic picture in which, they contended, sudden death frequently occurs even without an injection.

Henszelmann [66] also reported a fatality but did not believe that it was due to the mercurial. Molnár [67] described a man aged 39 who had ascites, syphilitic aortitis and aortic insufficiency. The patient was given 2 cc. of mercupurin intraperitoneally and complained of intense abdominal pain immediately after the injection. Twenty to twenty-five minutes later he became dyspneic and cyanotic and died. Autopsy revealed the presence of syphlitic aortitis but failed to explain the sudden death. Molnár believed, however, that his patient died because of hypersensitivity to the drug. In this regard, it is interesting to note that Petersen [42] injected salyrgan into the ascitic fluid in 7 cases. The administration of the drug by this method did not give any serious side reactions, but it was not of any advantage either, for it failed to give a protracted diuresis. Tyson [59] reported the death of a boy aged 3 years with severe anasarca from nephrosis. He received 0.5 cc. intravenously and one month later 1 cc. of mercupurin intravenously. As soon as the needle was withdrawn the patient had a generalized convulsion and gave an outcry. The heart beat could not be heard and respirations became slow and stertorous, and he died one minute after the injection. Partial necropsy revealed considerable congestion of the kidneys and typical changes of chronic lipoid nephrosis.

Two fatal cases following the use of mercupurin were reported by Lindberg and his associates,[63] but details of these cases are lacking. Vaughn [68] studied a 16 year old boy who had been deeply cyanosed since birth and in whom myocardial failure due to a congenital heart disease had developed. He was receiving digitalis and ammonium chloride and was given 2 cc. of mercupurin intravenously (which was practically synonymous with intra-arterial injection due to a patent ductus arteriosus). Within two minutes he complained of lumbar pain, became ashen gray and rapidly unconscious and died a respiratory death with severe dyspnea within four minutes of the time of completion of the injection. Hausheer's [69] patient was a woman aged 59 with hypertensive, arteriosclerotic heart disease and considerable renal involvement; she had been receiving digitalis, ammonium chloride and mercurial diuretics (salyrgan and mercupurin) for over three years. Owing to the better diuresis obtained with mercupurin, it was used exclusively during the latter part of her illness. She received from one to three intravenous injections of 2 cc. weekly. At the time of her last injection her condition seemed worse than usual; she was literally gasping for breath. Immediately following her usual injection she slumped over and died instantly without a gasp or effort of any kind.

Through the courtesy of the authors we are able to present the pertinent facts about the deaths reported by Friedfeld, Kissin, Modell and Sussman.[1] Friedfeld and Kissin's patient was a woman aged 52 with diabetes, hypertension and arteriosclerotic heart disease. In addition to the mercurial diuretic the patient was receiving digitalis and ammonium chloride. At first mercupurin was given intramuscularly, but because one injection was followed by a slough they changed, on the insistence of the patient, to the intravenous route. The first intravenous injection of 1 cc. of mercupurin was followed in from one to two minutes by a sudden paroxysm of urgent dyspnea and orthopnea. The heart rhythm remained regular and the blood pressure was unchanged. This episode lasted from two to three minutes and recurred at almost each succeeding injection despite all precautions. Since the patient persisted in her aversion to the intramuscular injections, and other efforts at diuresis were inadequate, the intravenous injections (increased to 2 cc.) were of necessity continued at five day intervals. About four

61. Sundaram, S. K.: Idiosyncrasy to Salygran, correspondence, J. A. M. A. **103**: 60 (July 7) 1934.
62. Hug, W.: München. med. Wchnschr. **82**: 184-185 (Jan. 31) 1935.
63. Lindberg, H.; Thomas, M., and Barker, M. N.: American College of Physicians meeting, Chicago, Dec. 6, 1941; personal communication to the authors.
64. A term used synonymously with salyrgan by Greenwald and Jacobson.[47]
65. Engel, K., and Epstein, T.: Orvosi hetil. **77**: 793-796 (Sept. 9) 1933.
66. Henszelmann, A.: Gyógyászat. **74**: 584-588 (Oct. 7) 1934.
67. Molnár, Stephan: Klin. Wchnschr. **14**: 239-240 (Feb. 16) 1935.
68. Vaughn, J. O.: Personal communication to the authors, 1940.
69. Hausheer, W. C.: Personal communication to the authors, 1941.

and one-half months after her first intravenous injection, following the injection of 2 cc. of mercupurin intravenously, she presented the usual reaction in about one minute. In another minute this seemed to subside and suddenly, about two to three minutes after the completion of the injection, her face flushed intensely and she collapsed. There were no convulsions. Her pulse was not obtainable and heart sounds were not heard. After a few gasps the patient was dead.

The patient observed by Modell had syphilitic heart disease and had received more than forty injections of mercupurin at weekly intervals with good diuretic response and no unpleasant or untoward reaction. She was also taking digitalis and ammonium chloride. Within about two minutes of completion of the last injection she became breathless, indicated distress in the region of her chest and fell over dead. Artificial respiration, intracardial epinephrine and cardiac massage were to no avail. The heart action had stopped before the respirations. There were no convulsions at any time.

Sussman's patient was a woman aged 60 with hypertension, arteriosclerotic heart disease and old coronary occlusion with persistent right and left sided heart failure. Other than the usual cardiac complaints, she had profuse sweats which seemed at times to be aggravated by intravenous diuretics. For the past year and a half she had been receiving digitalis, ammonium chloride and diuretics. Following her last intravenous injection of 2 cc. of mercupurin her face became flushed; she made an effort to speak but could only move her hands. Her heart rate slowed to 30 beats a minute and continued irregular. Respiration became infrequent, progressive cyanosis appeared and death took place within four minutes after the injection. Because of technical difficulty the injection prior to the last one was given intramuscularly.

Goldring and Sussman [70] furnished us with a report that a man aged 60 with arteriosclerotic heart disease and recent myocardial infarction in congestive failure had been given 1 cc. of mercupurin with good diuretic response. Twelve days later he was given a second injection of mercupurin, and three hours later he suddenly became dyspneic, syncope developed, and in a few seconds he died.

In reviewing these deaths certain significant facts are apparent. First, some deaths are obviously not the result of the mercurial diuretic, and in others the part that the diuretic may have played in the fatal outcome is decidedly questionable. Second, a large proportion of the deaths occurred in patients with evident kidney disease. It may have been necessary to use a mercurial diuretic in such cases, but the increased risk involved should certainly have been known prior to the injection of the drug. Mercurial diuretics are generally conceded to be contraindicated in kidney disease. Third, several patients had reactions of some type with a previous injection. Such reactions are warning signals of danger, and if mercurial diuretics must be given, then a change to another preparation is indicated. Fourth, some patients were practically moribund on admission. Any drug used might be blamed for the death; posthoc, propter hoc. Fifth, a small group of cases is left in which death unfortunately must be ascribed to the drug itself, and no precautions taken prior the injection could seemingly have prevented the fatal outcome. Further investigations on animals may lead to some information which may help to reduce even this small number.

70. Goldring, W., and Sussman, R. M.: Personal communication to the authors, 1942.

COMMENT AND SUMMARY

In a review such as this, one should not lose perspective. One must remember that the toxic reactions and deaths reported from mercurial diuretics are in reality only a small number in relation to the extensive use of these drugs. The low toxicity of the mercurial diuretics has been amply demonstrated by Wiseman,[71] Maxwell, Scott and Harvey,[72] Dixson,[73] Levine [74] and Fineberg.[75] At Bellevue Hospital approximately 6,000 injections, most of them intravenously, of mercurial diuretics are given every year. Since 1934, when mercupurin was first used in that hospital, we have known of no serious toxic reaction or death which might be attributed to the drug. Modell in a personal communication stated: "I might say that I personally have given over 2,000 injections of mercurial diuretics without any serious mishap prior to the one reported." A comparison with the arsphenamines used in the treatment of syphilis is illuminating. Hahn [76] recently reported an incidence of one death in twelve thousand injections of the arsphenamines. While we do not possess accurate statistics relating to the number of injections of mercurial diuretics administered, it can safely be assumed that well in excess of one hundred deaths a year would be attributed to these drugs if deaths occurred at the same rate as follow the use of the arsphenamines. Actually, there has been reported a total of twenty-six deaths from mercurial diuretics over a period of sixteen years.

No deaths have been reported from the administration of the mercurial diuretics intramuscularly or by rectum, but this may be due to the fact that the intravenous route is by far the commonest method used.

The human liver is apparently much less sensitive to mercurial diuretics than the liver of experimental animals, for though we have carefully looked for liver damage in our patients we failed to observe any. No case of aplastic anemia or granulocytopenia, such as is occasionally seen with mercury in the treatment of syphilis, has been reported in the literature or seen by us.

Circulatory disturbances, collapse, rigors, fever and more rarely the state suggestive of anaphylactic shock following the use of mercurials are occasionally seen by the intravenous injection of other substances, such as 10 per cent calcium chloride.[65] These reactions are probably no more common than with other potent drugs commonly employed and, although rare, they must be considered carefully in the treatment of a patient. It would seem that the organic portion of the molecule is of considerable significance in determining such a toxic reaction, since the several drugs differ decidedly in their lethal doses [2] and in their ability to produce reactions.[56] When a reaction occurs, another preparation should be cautiously tried. Changing the mode of administration with the same preparation does not seem to help.

Previous medication by digitalis may produce digitalis toxicity but not one of the characteristic mercurial

71. Wiseman, J. R.: The Prolonged Use of Salyrgan as a Diuretic, J. A. M. A. **99:** 114 (July) 1932.
72. Maxwell, E. S.; Scott, J. W., and Harvey, John: A Study of the Effect of Mercurial Diuretics on Kidney Disease, society proceedings, J. A. M. A. **101:** 2074 (Dec. 23) 1933.
73. Dixson, I. M.: New England J. Med. **210:** 800 (April 12) 1934.
74. Levine, S. A.: Clinical Heart Disease, Philadelphia, W. B. Saunders Company, 1936, p. 299.
75. Fineberg, M. H.: Am. Heart J. **17:** 494, 1939.
76. Hahn, R. D.: Am. J. Syph., Gonor. & Ven. Dis. **25:** 659, 1941.

reactions. If a mercurial diuretic must be given to a completely digitalized patient, it is advisable to discontinue the digitalis temporarily and remove as much fluid as possible by paracentesis before the mercurial diuretic is given.

As in the experimental animal, sudden death appears to be chiefly cardiac, probably ventricular fibrillation, although a few cases would suggest respiratory failure as well.

Mercurial diuretics are useful drugs, frequently indispensable, and it would indeed be unwise to restrict their clinical application on account of an occasional untoward reaction. It should be borne in mind, however, that these drugs are very potent and they must be used with due consideration to contraindications, associated medication such as digitalis, state of salt and water balance and previous reactions shown by the patient.

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PNEUMONIA IN ILLINOIS 1938-1941

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The use of highly refined antipneumococcus serum and the sulfonamide compounds has revolutionized the treatment of pneumonia. As most clinical reports have shown, these advances in treatment have occasioned a material reduction in the pneumonia fatality rate. Much of this remarkable achievement is the result of well organized pneumonia control programs conducted by public health agencies. Yet relatively few reports emanating from these agencies have appeared in the literature.

Our purpose in this paper is not only to present the results of the Illinois Pneumonia Control Program but also to encourage physicians in the use of such facilities, where they exist, to a greater degree. Although year by year a higher percentage of pneumonia patients have come under the Illinois Control Program, less than 50 per cent are now obtaining the services available.

Table 1 exhibits the history of pneumonia in Illinois during the last five years. In 1937, the year prior to the institution of the control program, there were 5,512 deaths, giving a fatality rate (per hundred cases reported) of 36.8 per cent. During the second year of pneumonia control activity there were 3,738 deaths, with a fatality rate of 25.6 per cent. The fatality rate of those cases treated under the program in 1940 was only 8.7 per cent. It would seem reasonable to assume that the lowered pneumonia mortality rate during 1940 in Illinois was due largely to improved methods and facilities for the treatment of this disease. The advent of therapeutic serum and drugs was undoubtedly the principal factor in the reduction of mortality. However, this result could not have been accomplished without the facilities of the control program. The program not only acquainted the physician with the modern methods of treatment but also furnished him with free diagnostic services and therapeutic materials. These services were available free of cost for all patients with pneumonia regardless of their financial status.

Dr. Roland R. Cross, Director, Illinois Department of Public Health, Dr. J. J. McShane, Chief, Division of Communicable Diseases, Illinois Department of Public Health, and the members of the Illinois Pneumonia Advisory Board cooperated in making this study possible. Valuable clerical assistance in processing data was furnished by the Work Projects Administration.

ORGANIZATION OF THE ILLINOIS PNEUMONIA CONTROL PROGRAM

Prior to 1938 there had been no concerted effort to control pneumonia in Illinois. In November 1938 the Illinois Department of Public Health with the cooperation of the United States Public Health Service inaugurated a statewide program for the control of this disease. During the first year pneumococcus typing stations as well as distributing centers for serum and drugs were established. An extensive educational program was undertaken to familiarize the physicians and the public at large with the new facilities available for the treatment of pneumonia. At first only horse serum for the common types of pneumococcic pneumonia was available. As concentrated rabbit serum and, later, the sulfonamide compounds were proved efficient by clinical trial, these were also made available for free distribution to all patients with pneumonia.

Progress was rapid, and by 1940 there were one hundred and sixty private and state agencies approved to perform pneumococcus typing and twenty-seven strategically located centers authorized to distribute serum and drugs. In 1940 the number of typing stations was increased to one hundred and eighty and the serum centers to thirty-seven. For more efficient and rapid distribution the sulfonamide compounds (sulfapyridine and sulfathiazole) were made available at all the pneumococcus typing stations as well as at the serum centers. This extensive distribution system provided every area of the state, rural and urban, with readily available specific agents for the treatment of pneumonia. The geographic distribution of the pneumonia control centers is exhibited by the accompanying map.

TABLE 1.—*Pneumonia in Illinois 1935-1941*

Year	Cases Reported	Deaths	Fatality Rate *
1935	13,519	5,984	44.3
1936	15,926	6,312	39.6
1937	14,970	5,512	36.8
1938	12,834	4,595	35.8
Illinois Pneumonia Control Program inaugurated November 1938			
1939	13,472	4,193	31.1
1940	14,592	3,738	25.6
Results of Illinois Pneumonia Control Program			
Jan. 1, 1939-June 30, 1939	1,448	222	15.3
July 1, 1939-June 30, 1940	6,348	539	8.5
July 1, 1940-June 30, 1941	7,652	664	8.7

* Per hundred cases reported.

COLLECTION OF DATA

Source of the Data.—All physicians utilizing diagnostic services or obtaining therapeutic materials from approved pneumonia control centers were required to submit a "physician's pneumonia case report." The physicians cooperated splendidly, and satisfactory reports were obtained for over 90 per cent of the cases. To simplify analysis of results, these reports were abstracted and the pertinent information was punched on eighty-column cards. Tabulating machines were then used to prepare the reports. Cases in which

the diagnosis of pneumonia was doubtful or in which the outcome was not determinable from the history were eliminated from the series.

Limitations of the Data.—Case reports were often incomplete, so that many cases had to be eliminated from certain analyses for lack of information on age, interval from onset until beginning of treatment and number of lobes involved. Since case reports originated from many sources, they varied not only in completeness but also in the interpretation of many items. There seems to be no reason, however, to believe that the accuracy and completeness of reporting varied significantly in the groups of patients receiving different kinds of treatment. It is well recognized that there may be selective factors for the group receiving serum and chemotherapy, since it is common knowledge that patients who fail to show a satisfactory response to drug alone are often given serum later.

Geographic distribution of pneumonia control centers in Illinois in 1941.

RESULTS

From November 1938 to July 1941 there were 15,448 pneumonia case histories received by the Section of Pneumonia Control under the program. Among the 15,448 cases there were 1,425 deaths, giving a fatality rate (per hundred cases reported) of 9.2 per cent; 13,160 of these cases were due to the pneumococcus (table 2). In this group there were 1,200 deaths, giving a fatality rate of 9.1 per cent. Types 1, 3, 2 and 7 were the most prevalent types encountered and together accounted for 41 per cent (6,409) of all cases and 42 per cent (602) of all deaths. The other common types (8, 6, 4, 19, 5 and 14, in order of their prevalence) accounted for 22.1 per cent (3,409) of all cases and 19.4 per cent (277) of all deaths. In 277 cases a pneumococcus was isolated but could not be classified by the Neufeld quellung reaction and other diagnostic tests into the thirty-three types for which serum was available.

It should be mentioned that more than 10 per cent of all specimens submitted were from children in Cook County Hospital. Thus the relative incidence of types 6, 14 and 19, which are most commonly found in children, is perhaps higher in this series than in others reported.

In this series there were 2,288 cases of non-pneumococcic pneumonia with 225 deaths, giving a fatality rate of 9.9 per cent. A streptococcus was the apparent etiologic agent [1] in 972 cases. Hemolytic streptococci accounted for 217 cases, Streptococcus viridans for 262 cases and unclassified streptococci for 493 cases. The respective fatality rates were 10.1, 9.5 and 11.2 per cent. In 134 cases in which staphylococci [2] were isolated there were 26 deaths, giving a fatality rate of 19.4 per cent. No laboratory report was received for 1,156 cases, in which there were 91 deaths, giving a fatality rate of 7.9 per cent.

In 1,515 cases more than one organism was isolated from the specimen submitted. In this group there were 160 deaths, giving a fatality rate of 10.6 per cent.

It has been definitely shown by numerous investigators that certain factors influence the outcome of pneumonia. Our results corroborate these observations, and from the data accumulated we are able to show strikingly the important roles played by several factors. These are (1) age, (2) bacteremia, (3) number of lobes involved, (4) day treatment begun and (5) complications.

Influence of Age on Outcome.—Data on the effect of age on the outcome of pneumonia are shown in table 3. The results obtained are in agreement with present knowledge of the disease, namely that the prognosis becomes graver as age increases despite the form of treatment used. We may divide our series into three age groups: under 2 years of age, 2 to 39 years and 40 and over. The respective number of cases and fatality rate are as follows: under 2 years of age 1,398 cases with 103 deaths (7.4 per cent), 2 to 39 years of age 7,296 cases with 257 deaths (3.5 per cent) and over 40 years of age 6,500 cases with 1,034 deaths (15.9 per cent). It should be pointed out that apparently age played an important role in the choice of therapy. Among patients over 40 years of age 3,178 received combined treatment, as compared with 2,479 who received drug alone. In contradistinction, among patients under 40 years of age, including infants, 3,082 received serochemotherapy while 4,593 received drug alone.

Effect of Bacteremia and Lobar Involvement on the Outcome.—Although blood cultures were reported for only one fourth of all cases, the 4,140 cultures in this series constitute a sufficient sample to warrant definite conclusions. Of the 4,140 blood cultures, 811 (19.5 per cent) were positive. Of the 811 cases in which the cultures were positive there were 208 deaths, giving a fatality rate of 25.6 per cent. On the other hand, only

1. Streptococci were reported on the bacteriologic report as the predominant organism. It should be emphasized that these figures represent the predominant organism isolated from sputum, throat swabs and so on. Streptococci, particularly Streptococcus viridans and unclassified streptococci, may or may not be true etiologic agents, since these organisms are frequently found in the upper respiratory tract of normal persons.

2. The etiologic significance of staphylococci in these cases may be questioned.

269 deaths occurred among the 3,329 cases in which the blood cultures were negative, a fatality rate of 8.1 per cent.

That the number of lobes involved is an index to the severity of pneumonia is also shown in table 4. Single lobe involvement was twice as frequent as multiple lobe involvement, there being 8,482 and 4,704 cases respectively. The fatality rate of 15.7 per cent for cases of multiple lobe involvement was approximately three times as great as the rate (5.7 per cent) for cases of single lobe involvement. In 2,262 cases the number of lobes involved was not reported. In this group there were 203 deaths, giving a rate of 9 per cent.

Influence of Delayed Treatment on Outcome.—Our results corroborate the well known fact that the efficacy of any form of pneumonia therapy is decidedly diminished when treatment is delayed. Of the patients with pneumococcic pneumonia for whom all pertinent data relating to prognostic factors [3] were obtained and who received serum or chemotherapy, 1,963 were treated after the fourth day, with 231 deaths (11.8 per cent fatality rate), as compared with 7,601 treated on or before the fourth day, with 616 deaths (8.1 per cent fatality rate). This is shown in table 6.

Effect of Complications and Associated Diseases on Outcome.—As might be expected, patients with complications and associated diseases were definitely poorer risks. Of those who received combined treatment there were 1,685 with complications or associated diseases; of this group 444 died (26.4 per cent fatality rate).

TABLE 2.—*Pneumonia Morbidity and Fatality Classified According to Kind of Treatment for Each Type of Organism*

Laboratory Result *	All Treatments			Chemotherapy and Serum			Chemotherapy (No Serum)			Serum (No Chemotherapy)			No Chemotherapy or Serum		
	Cases	Deaths	Rate †	Cases	Deaths	Rate †	Cases	Deaths	Rate †	Cases	Deaths	Rate †	Cases	Deaths	Rate †
Pneumococcus type 1	2,453	153	6.2	1,408	94	6.7	701	20	2.9	294	28	9.5	50	11	22.0
Pneumococcus type 2	1,317	134	10.2	724	78	10.8	414	25	6.0	155	22	14.2	24	9	37.5
Pneumococcus type 3	1,622	250	15.4	1,013	171	16.9	461	41	8.8	69	18	26.1	76	20	26.3
Pneumococcus type 4	557	53	9.5	291	36	12.4	189	6	3.2	56	7	12.5	21	4	19.0
Pneumococcus type 5	493	35	7.1	239	25	10.5	189	4	2.1	48	4	8.3	17	2	11.8
Pneumococcus type 6	611	50	8.2	205	30	14.6	330	11	3.3	17	5	29.4	59	4	6.8
Pneumococcus type 7	1,017	65	6.4	528	37	7.0	344	12	3.5	113	9	8.0	32	7	21.9
Pneumococcus type 8	807	71	8.8	451	41	9.1	231	13	5.6	90	13	14.4	35	4	11.4
Pneumococcus type 9	202	18	8.9	99	8	8.1	84	6	7.1	10	3	30.0	9	1	11.1
Pneumococcus type 10	158	15	9.5	66	9	13.6	73	3	4.1	4	0	0.0	15	3	20.0
Pneumococcus type 11	211	23	10.9	89	11	12.4	100	7	7.0	6	2	33.3	16	3	18.8
Pneumococcus type 12	119	11	9.2	43	3	7.0	67	6	9.0	7	1	14.3	2	1	50.0
Pneumococcus type 13	161	20	12.4	57	10	17.5	88	6	6.8	5	1	20.0	12	3	25.0
Pneumococcus type 14	436	22	5.0	160	8	5.0	236	11	4.7	23	1	4.3	16	2	12.5
Pneumococcus type 15	176	22	12.5	50	6	12.0	109	10	9.2	3	3	100.0	14	3	21.4
Pneumococcus type 16	151	24	15.9	60	13	21.7	68	7	10.3	12	3	25.0	11	1	9.1
Pneumococcus type 17	200	21	10.5	80	11	13.8	102	6	5.9	8	2	25.0	10	2	20.0
Pneumococcus type 18	257	24	9.3	88	9	10.2	131	7	5.3	15	4	26.7	23	4	17.4
Pneumococcus type 19	505	46	9.1	195	25	12.8	245	10	4.1	25	5	20.0	40	6	15.0
Pneumococcus type 20	247	26	10.5	80	13	16.2	146	11	7.5	5	0	0.0	16	2	12.5
Pneumococcus type 21	109	9	8.3	35	6	17.1	67	1	1.5	3	2	66.7	4	0	0.0
Pneumococcus type 22	151	13	8.6	61	9	14.8	74	2	2.7	5	2	40.0	11	0	0.0
Pneumococcus type 23	189	17	9.0	70	8	11.4	93	5	5.4	9	2	22.2	17	2	11.8
Pneumococcus type 24	123	10	8.1	44	9	20.5	63	0	0.0	10	0	0.0	6	1	16.7
Pneumococcus type 25	55	4	7.3	17	2	11.8	29	1	3.4	1	0	0.0	8	1	12.5
Pneumococcus type 26	4	0	0.0	0	0	....	4	0	0.0	0	0	....	0	0	....
Pneumococcus type 27	47	1	2.1	18	0	0.0	24	1	4.2	2	0	0.0	3	0	0.0
Pneumococcus type 28	126	12	9.5	43	8	18.6	67	3	4.5	4	1	25.0	12	0	0.0
Pneumococcus type 29	123	11	8.9	44	4	9.1	58	5	8.6	7	1	14.3	14	1	7.1
Pneumococcus type 30	1	0	0.0	0	0	....	1	0	0.0	0	0	....	0	0	....
Pneumococcus type 31	91	7	7.7	36	2	5.6	38	2	5.3	6	2	33.3	11	1	9.1
Pneumococcus type 32	34	3	8.8	16	2	12.5	14	0	0.0	0	0	....	4	1	25.0
Pneumococcus type 33	130	7	5.4	35	2	5.7	78	1	1.3	8	2	25.0	9	2	22.2
Pneumococcus, unclassified	277	23	8.3	2	0	0.0	239	18	7.5	0	0	....	36	5	13.9
Friedländer's bacillus type A	8	1	12.5	0	0	....	7	1	14.3	0	0	....	1	0	0.0
Friedländer's bacillus type B	5	3	60.0	0	0	....	5	3	60.0	0	0	....	0	0	....
Friedländer's bacillus, unclassified	13	2	15.4	0	0	....	11	2	18.2	0	0	....	2	0	0.0
Staphylococcus aureus	80	12	15.0	0	0	....	71	11	15.5	0	0	....	0	0	....
Staphylococcus albus	14	3	21.4	0	0	....	11	3	27.3	0	0	....	3	0	0.0
Staphylococcus, unclassified	40	11	27.5	0	0	....	32	8	25.0	0	0	....	8	3	37.5
Streptococcus hemolyticus	217	22	10.1	1	0	0.0	192	20	10.4	0	0	....	24	2	8.3
Streptococcus viridans	262	25	9.5	1	0	0.0	236	20	8.5	0	0	....	25	5	20.0
Streptococcus, unclassified	493	55	11.2	3	0	0.0	401	43	10.7	1	0	0.0	88	12	13.6
No laboratory result	1,156	91	7.9	2	0	0.0	1,055	70	6.6	1	1	100.0	98	20	20.2
All cases	15,448	1,425	9.2	6,354	690	10.9	7,181	442	6.2	1,022	144	14.1	891	149	16.7

* If more than one type was reported for a case and there was no indication as to predominant type, the case is classed in this table under the lowest type number.

† Per hundred cases reported.

TABLE 3.—*Influence of Age on Pneumonia Morbidity and Mortality*

Age of Patient, Years	All Treatments			Chemotherapy and Serum		Chemotherapy (No Serum)		Serum (No Chemotherapy)		No Chemotherapy or Serum	
	Cases	Deaths	Rate *	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Under 2	1,398	103	7.4	281	38	1,003	47	26	4	88	14
2-9	2,203	46	2.1	536	13	1,449	24	66	3	152	6
10-19	1,270	27	2.1	487	7	630	13	100	2	83	5
20-29	1,730	65	3.8	774	23	715	26	161	7	78	9
30-39	2,093	119	5.7	1,004	65	826	32	170	14	93	8
40-49	2,066	221	10.7	962	113	844	64	166	21	94	23
50-59	1,895	261	13.8	963	137	687	69	133	29	112	26
60-69	1,425	278	19.5	688	133	545	83	112	35	80	27
70 or over	1,114	274	24.6	565	151	403	73	64	27	82	23
Unknown	254	31	12.2	94	10	109	11	22	2	29	8
All cases	15,448	1,425	9.2	6,354	690	7,181	442	1,022	144	891	149

* Per hundred cases reported.

3. Prognostic factors included age, day of disease treatment was begun, lobes involved and complications.

Among 3,604 patients without complications or associated diseases who received combined treatment only 139 died, a rate of 3.8 per cent. Similarly, of patients treated with the drug alone 613 had complications and 102 died, a fatality rate of 16.6 per cent, as compared with 2,839 patients with uncomplicated pneumonia, of whom 53 died, a rate of 1.9 per cent.

COMPARISONS OF METHODS OF TREATMENT

At present much interest is focused on the comparative value of serum plus drug versus sulfonamide compounds alone in the treatment of pneumonia. The pneumonia control programs should give valuable aid in the solution of this problem.

In the absence of adequate controls a valid comparison of therapeutic procedures must allow for compositional differences among the groups considered with respect to factors affecting outcome. Thus, some of the apparent superiority of drug therapy alone over the combined method is certainly due to the fact that the patients receiving the combined therapy were more seriously ill.

The severity of illness in these patients cannot be measured accurately with present methods. Until the time when precise methods of determining severity of pneumonia are available, one must be content to measure severity by the presence or absence of prognostic factors.

Table 5 shows how the various treatment groups in this study were composed with respect to certain prognostic factors. The factors considered were age, day of disease on which treatment was begun, lobe involvement and complications.

Each of the four factors was divided into only two categories, because otherwise a prohibitive number of classes would have been obtained in the process of cross classification. The group having complications is espe-

TABLE 4.—*Influence of Bacteremia and Lobar Involvement on Mortality*

Number of Lobes Involved	Blood Culture: Total Cases	Total Deaths	Total Rate ‡	Positive * Cases	Positive * Deaths	Negative † Cases	Negative † Deaths	No Record Cases	No Record Deaths
1	8,482	483	5.7	429	91	2,073	83	5,980	309
2	3,308	419	12.4	233	63	675	82	2,400	274
3	920	203	22.1	71	29	187	51	662	123
4	203	56	27.6	14	4	32	10	157	42
5	213	61	28.6	6	5	46	18	161	38
Not given	2,262	203	9.0	58	16	316	25	1,888	162
All cases	15,448	1,425	9.2	811	208 (25.6 ‡)	3,329	269 (8.1 ‡)	11,308	948 (8.4 ‡)

* At least one positive blood culture. † No positive blood culture but at least one negative. ‡ Per hundred cases reported.

TABLE 5.—*Influence of Age, Time of First Treatment, Number of Lobes Involved and Complications to Morbidity and Fatality in Relation to Kind of Treatment*

Treatment Begun	Involvement of Lobes	Complications *	All Treatments: Cases	Deaths	Rate †	Chemotherapy and Serum: Cases	Deaths	Rate †	Chemotherapy (No Serum): Cases	Deaths	Rate †	Serum (No Chemotherapy): Cases	Deaths	Rate †	No Chemotherapy or Serum: Cases	Deaths	Rate †
Age 40 years and over																	
After fourth day from onset	Two or more	Yes	198	96	48.5	143	68	47.6	39	17	43.6	12	8	66.7	4	3	75.0
		No	210	28	13.3	109	16	14.7	75	8	10.7	23	1	4.3	3	3	100.0
	One	Yes	175	47	26.9	86	26	30.2	79	14	17.7	8	5	62.5	2	2	100.0
		No	385	17	4.4	153	10	6.5	197	4	2.0	31	3	9.7	4	0	0.0
On or before fourth day from onset	Two or more	Yes	545	226	41.5	403	166	41.2	81	27	33.3	59	31	52.5	2	2	100.0
		No	804	70	8.7	535	50	9.3	194	9	4.6	70	8	11.4	5	3	60.0
	One	Yes	628	139	22.1	428	96	22.4	142	22	15.5	56	21	37.5	2	0	0.0
		No	1,480	57	3.9	857	32	3.7	476	14	2.9	134	8	6.0	13	3	23.1
Age under 40 years																	
After fourth day from onset	Two or more	Yes	95	23	24.2	65	20	30.8	22	1	4.5	7	1	14.3	1	1	100.0
		No	227	10	4.4	92	3	3.3	115	3	2.6	16	2	12.5	4	2	50.0
	One	Yes	122	18	14.8	61	11	18.0	49	5	10.2	10	1	10.0	2	1	50.0
		No	576	4	0.7	161	4	2.5	371	0	0.0	39	0	0.0	5	0	0.0
On or before fourth day from onset	Two or more	Yes	292	51	17.5	206	32	15.5	60	10	16.7	23	8	34.8	3	1	33.3
		No	971	24	2.5	522	11	2.1	334	8	2.4	98	5	5.1	17	0	0.0
	One	Yes	468	34	7.3	293	25	8.5	141	6	4.3	32	3	9.4	2	0	0.0
		No	2,473	24	1.0	1,175	13	1.1	1,077	7	0.6	205	4	2.0	16	0	0.0
All cases ‡			9,649	863	9.0	5,289	583	11.0	3,452	155	4.5	823	109	13.2	85	21	24.7

* A case was included in the "Yes" group under "Complications" if at least one of the following items was indicated on the history: alcoholism, bacteremia, diabetes, empyema, heart disease, lung abscess, meningitis, nephritis, pleural effusion, postoperative pneumonia, pregnancy and tuberculosis. It is quite possible that cases of unreported complications are included in the groups classified as having no complications.

† Per hundred cases reported.

‡ This table includes only the cases for which all of the following items were reported: type of pneumococcus, patient's age, number of lobes involved and time of first treatment in relation to onset of the disease. There were 7,799 other cases for which some of the items were not reported.

results of laboratory studies show that in general the ideal treatment of pneumonia should include both specific serum and drug. Clinical studies to date, however, have not substantiated this view. The solution of the problem, as Bullowa [4] has stated, will come only after observation of many patients over a period of years. The clinical and statistical studies arising from effective

4. Bullowa, J. G. M.; Osgood, E. E.; Bukantz, S. C., and Brownlee, I. E.: The Effect of Sulfapyridine Alone and with Serum on Pneumococcic Pneumonia and on Pneumococcus Infected Marrow Cultures, Am. J. M. Sc. **199**: 364-380 (March) 1940.

cially heterogeneous. It is recognized that some of our classifications could be improved, particularly by a fuller use of the information available on the amount of drug or serum used, the time of the first treatment and the duration of treatment. A higher proportion of serious cases was found to exist among the patients receiving combined drug and serum treatment than among those treated with drug alone. This is shown by the relative numbers of patients classified in the group of greatest severity of disease, namely persons over 40 with two or more lobes involved and complications present. Out of 666 patients in this category, 546 were treated with both drug and serum and 120 with drug only. Thus, among these seriously ill patients there was a selection of 4½ to 1 in favor of combined therapy. Other classifications relating disease severity to age, number of lobes involved and complications all show that in the presence of unfavorable prognostic factors drug plus serum were more apt to be given than drug alone. Thus, in patients over 40 years of age 51 per cent received combined treatment and 37 per cent chemotherapy only. In cases with multiple lobe involvement 39 per cent were given drug and serum while only 27 per cent were treated with drug alone. Similarly among patients with complications the ratio was combined therapy 32 per cent, drug only 18 per cent. The one adverse prognostic factor present to a greater degree in the cases in which only chemotherapy was administered was that of treatment begun after the fourth day of the disease, e. g. combined therapy 16 per cent, drug alone 27 per cent. It is probably of considerable importance to note in this same table 5 that of type 3 pneumonias 62 per cent had combined treatment as compared with 29 per cent who received only drug. The number of patients not given chemotherapy was so small that the percentages for these groups are, in general, insignificant.

Comparisons by Adjusted Fatality Rates. — As already shown, the patients in the group receiving combined therapy were not distributed in the same way with respect to prognostic factors as the patients receiving sulfonamide compounds alone. To offset these differences adjusted fatality rates [5] for each factor are exhibited in table 7.

TABLE 6.—*Influence of Delayed Treatment on Outcome*

Treatment	Treated On or Before Fourth Day			Treated After Fourth Day		
	Number	Deaths	Mortality Rate *	Number	Deaths	Mortality Rate *
Combined treatment	4,419	425	9.6	870	158	18.2
Drug alone	2,505	103	4.1	947	52	5.5
Serum alone	677	88	13.0	146	21	14.4
Totals	7,601	616	8.1	1,963	231	11.8

* Per hundred cases reported.

The adjusted rates are derived from the data of table 5 by first estimating the deaths to be expected among patients in each of the sixteen prognostic factor combinations if all patients with a given combination of prognosis items had received the same treatment. For example, in the first prognostic factor group of 198 cases, on applying the fatality rate of 43.6 per cent for the patients receiving chemotherapy alone 83.6 estimated deaths are obtained. Thereupon the adjusted rates are computed from the expected deaths. Thus a comparison of the two methods of treatment by adjusted rates is in effect a comparison based on a standard group of patients. It is readily seen that a large part of the difference between treatments in the crude fatality rates is due to the variation in composition between the group receiving combined therapy and that receiving chemotherapy alone. The crude fatality rate of 11 per cent for the group receiving both serum and drug is two and one-half times as high as the rate for the group receiving drugs alone (4.5 per cent), while the adjusted rate is only one and one-half times as high (9.4 per cent and 6.6 per cent respectively).

5. A detailed description of such adjustment procedure is given by Pearl, Raymond: Introduction to Medical Biometry and Statistics, ed. 3, Philadelphia and London, W. B. Saunders Company, 1940, chapter IX.

TABLE 7.—*Comparison of Combined Treatment with Drug Therapy Alone in Regard to Factors of Age, Lobar Involvement, Time of First Treatment and Complications as Shown by Adjusted Fatality Rates*

Prognostic Factors	Number of Cases	Adjusted Fatality Rate *	
		Combined Treatment	Drug Alone
Age 40 or over	4,425	15.8	11.5
Age under 40	5,224	3.9	2.5
More than one lobe involved	3,342	15.8	12.3
Only one lobe involved	6,307	6.0	3.6
Treatment begun after fourth day from onset	1,988	13.9	8.8
Treatment begun on or before fourth day from onset	7,661	8.2	6.1
With complications	2,523	25.7	19.1
Without complications	7,126	3.6	2.2
All cases	9,649	9.4	6.6
Crude death rate * for all cases		11.0	4.5

* Per hundred cases reported.

SUMMARY

1. The Pneumonia Control Program of the Illinois Department of Public Health was initiated in November 1938. From this date to July 1, 1941, 15,448 cases of pneumonia were reported to the Section of Pneumonia Control. Among this number there were 1,425 deaths, giving a case fatality rate of 9.2 per cent. Of this group 13,160 were due to pneumococcus types 1-33, and all but 597 received chemotherapy, serum or both; 1,200 of the total group died, giving a mortality of 9.1 per cent.

2. The most common types of pneumococci in order of their prevalence were 1, 3, 2 and 7. The case fatality rates of these four types were 6.2, 15.4, 10.2 and 6.4 per cent respectively.

3. Cases were studied with reference to prognostic factors, namely age, day of disease treatment was begun, lobe involvement and complications.

4. An attempt was made to assess the value of treatment with serum and chemotherapy by allowing for the combined effects of these four prognostic factors.

5. While the death rate among patients treated with both serum and drug was more than twice that resulting from chemotherapy alone, it was found that the great majority of the most severely ill patients were selected for combined therapy.

6. Further statistical analyses are being undertaken with the purpose of elucidating as far as possible the value of combining serum with sulfonamides in the treatment of pneumonia.

Clinical Notes, Suggestions and New Instruments

ZINC DERMATITIS: AN ADDITIONAL HAZARD IN THE AIRCRAFT INDUSTRY

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The salts of zinc, such as zinc chloride, are widely used in welding in large plane manufacturing, and reactions to these compounds have been reported.[1] However, no recorded instance of reaction to zinc has been found, and I have no previous knowledge of such allergic reaction.

"Kirksite"[2] is an alloy which is used in the foundry in the preliminary stages of die making. It is composed principally of zinc with a small admixture of aluminum and copper and a lesser amount of magnesium.

At this time of national emergency it seems desirable to record the following case, although it is readily acknowledged that such cases will be rarely encountered:

REPORT OF CASE

K. W. W., a man aged 33, was referred for dermatologic consultation by Dr. M. L. Loomis, of the Long Beach medical division of the Douglas Aircraft Company, Inc. The patient was of English descent. His past history was irrelevant. The family history, though, was of interest. He stated that his grandmother, mother and father were sensitive to zinc and galvanized metals. His mother, for instance, could never use zinc coated buckets or tubs for such tasks as laundering without having a dermatitis develop on the exposed parts. There were no other known instances of allergic reactions in the patient or his near relatives.

This man suffered a burn from a splash of hot kirksite in the bend of the left elbow, and around this, while it was healing, developed an inflammation. Zinc oxide, among other ointments, had been used in the preliminary treatment of the burn.

Examination showed a healing burn about 2 cm. in diameter in the left cubital space. There was an erythematovesicular and exudative eruption extending around this slightly keloidal area for 3 cm. in each direction.

The Wassermann reaction of the blood was negative, and the urine was normal.

Patch tests with scrapings of kirksite showed, after fifteen hours, a severe erythema on which a small vesicular eruption was superimposed. The results of a control test were negative.

Improvement was definite but fairly slow, while therapy consisted in roentgen radiation and the application of sulfanilamide and bismuth tribromphenate in a cream locally, and it was more rapid when weak silver nitrate compresses were used. Alibour water (water containing zinc and copper sulfates) was carefully avoided. During treatment, when the patient was away from the plant considerable improvement would be noticed, and when he would return the involved areas would become pruritic "in about thirty minutes." For this reason it was necessary for Dr. Loomis to have him transferred from the foundry to another department where there would be no exposure to zinc.

After the eruption had entirely healed, and thirty-four days after the original patch test had been applied, patch tests with the constituents of kirksite were applied. Those with aluminum, magnesium and copper gave negative results after forty-eight hours, while that with zinc showed, after eighteen hours, a bullous reaction, which later became a 5 mm. deep slough and required another two weeks to heal.

At the time of the last mentioned reaction edema, erythema and pruritus occurred at the sites of the original patch test with kirksite on the same (right) forearm and of the original dermatitis on the left arm.

COMMENT

Sensitivity to zinc must be regarded as very rare. It has been suggested[3] that the dermatitis may have been due to the formation of zinc chloride from zinc reacting with perspiration. This cannot be disproved, as of course perspiration would occur under a patch test, but it is true that similar scrapings of kirksite have been applied as patch tests on several other persons without inducing any reaction. Zinc chloride is a primary irritant, and these negative results in other persons would indicate that there was a true zinc sensitivity in this case and that the reaction was not due to zinc chloride.

The flare-up at the previously involved sites when the zinc patch test was applied emphasizes the truly allergic nature of the reaction. This phenomenon has been previously described as the recurrent patch test reaction.[4]

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Dr. Freeman is now a captain in the Medical Corps and temporarily at the Johns Hopkins School of Hygiene, Baltimore.

1. Schwartz, Louis, and Russell, John P.: Skin Hazards in Airplane Manufacture, Pub. Health Rep. **56**: 1581-1593 (Aug. 8) 1941.

2. "Kirksite" is supplied by Morris P. Kirke & Son, Inc., Los Angeles.

3. Personal communication from Dr. Louis Schwartz, chief of the Dermatoses Investigation Section of the United States Public Health Service.

4. Counter, Clement E.: Recurrent Reaction to Patch Test, Arch. Dermat. & Syph. **37**: 495-496 (March) 1938.

RENAL TORSION WITH ISCHEMIA CAUSING HYPERTENSION

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AND
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This report is presented because of its unusual bearing on renal hypertension. The major implications seem consistent with scientific validity.

Since Goldblatt's work, impetus has been given to research on hypertension, and a great many articles have been written on the association of disorders of the kidney to high blood pressure. McCann[1] postulated the following events in cases of nephroptosis exhibiting orthostatic hypertension:

"1. Erect posture causes some slight interference with the afferent blood supply in consequence of which renin is produced.

"2. The action of renin results in constriction of the vasa efferentia in both kidneys with the result that the total renal blood flow is still further decreased, while at the same time the glomerular filtration remains relatively constant, owing to the compensatory effect of increased intraglomerular pressure."

In his series of 5 cases in which nephropexy was performed or kidney belts were applied the hypertension still existed to a lesser degree, but symptomatically there was much improvement.

REPORT OF CASE

A well developed woman aged 47, first seen Nov. 7, 1938, complained of severe headaches, nervousness and severe hot flashes. The headaches, which had become much more severe during the last three months, started one week before the expected menstrual period and lasted throughout. These symptoms had been present for two years but had been milder. The menses had become scanty during the past two years but were still regular every twenty-eight days. Physical examination was essentially negative except for a blood pressure reading of 180 systolic and 110 diastolic. Urinalysis was entirely negative. The impression at this time was that the climacteric had started, and until March 1939 estrogenic substances in the form of theelin and amniotin were given. During this period the blood pressure varied from 170/100 to 190/100.

1. McCann, W. S., and Romansky, M. J.: Orthostatic Hypertension, J. A. M. A. **115**: 573 (Aug. 24) 1940.

The flashes and nervousness were greatly relieved and the headaches were milder.

In September the patient complained of dizzy spells, tiredness, fatigue and swelling of the ankles. For the past two months she had been menstruating profusely every eighteen days. A second degree anemia was noted. Vaginal examination revealed a small, normal, anteflexed uterus. Roentgen therapy was instituted for the menorrhagia, and complete cessation of the menses occurred by December 15. The blood pressure was 180/100.

The patient felt well until Jan. 20, 1940, when she again complained of severe occipital and frontal headaches that came on at frequent intervals and were associated with nausea and vomiting. Hot flashes became intense, thirty to forty a day. The blood pressure was 180/100; otherwise physical examination was negative. Estrogenic therapy was reinstituted, large doses being given with relief of the flashes but no apparent relief of the headaches; morphine sulfate ¼ grain (0.016 Gm.) and soluble pentobarbital 4 to 6 grains (0.26 to 0.4 Gm.) were taken for relief. The blood pressure at this time was 220/120. A mixture of theobromine and phenobarbital was given as a vasodilator but caused no effect on the headaches or blood pressure. Urinalysis was still negative, nonprotein nitrogen of the blood was 40.8 mg. and creatinine 1.2 mg. The climacteric symptoms were controlled with 1 mg. of diethylstilbestrol daily. Complete bed rest was instituted, the patient improved and the blood pressure dropped to 180/190. Bed rest in a completely horizontal position relieved the patient to a great extent.

In September 1940 tenderness was noted for the first time over the left kidney region, and a genitourinary study was advised. The only other urologic symptoms were nocturia one to three times and a dull pain over the left kidney. A memory of attacks of kidney trouble twenty-five years previously was elicited; otherwise the past history was negative.

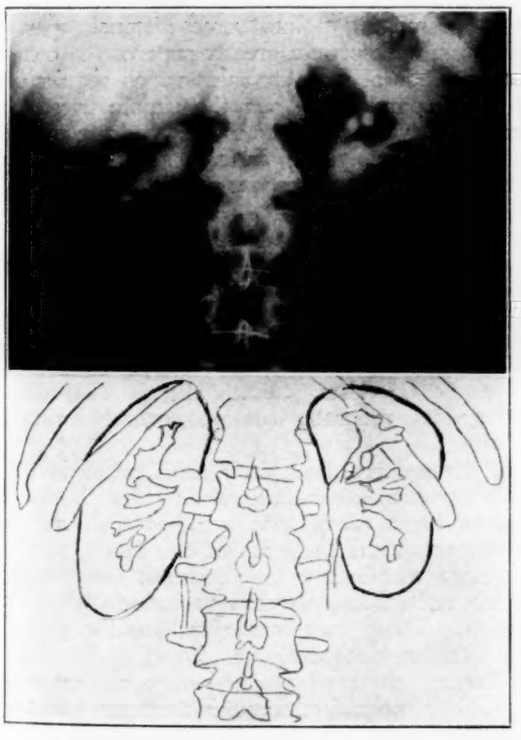

Fig. 1.—Normal extrarenal pelves, horizontal.

The blood pressure prior to urologic study was 240/120. The essential cystoscopic observations were that a number 6 catheter passed to the right pelvis easily but met resistance in the entire length of the left ureter. Phenolsulfonphthalein appeared in three minutes and in excellent concentration from both sides. Urine from both the right and the left kidney was normal. The retrograde pyelogram revealed normal appearing extrarenal pelves. In the upright position on the right side a torsion of 45 to 60 degrees of the pelvis was noted while the left side showed delayed emptying time, probably owing to the narrowing of the left ureter. The diagnosis of torsion of the right kidney

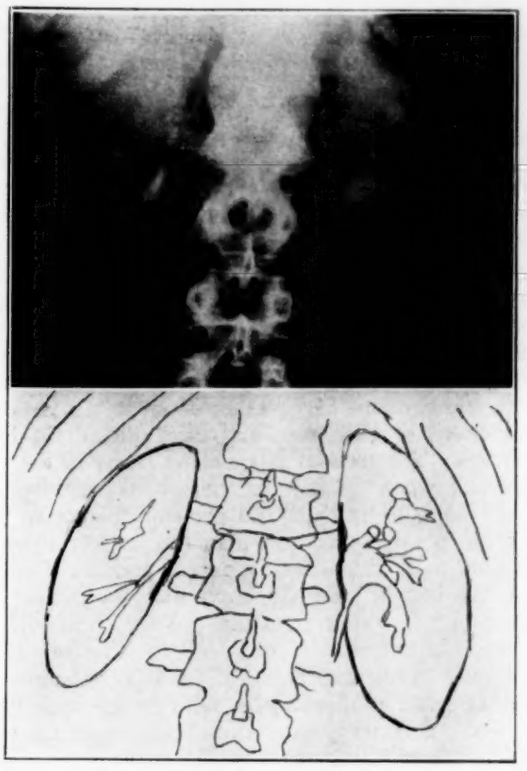

Fig. 2.—Torsion of right kidney in upright position.

and narrowing of the left ureter was made. Basing our supposition on the fact that torsion of the right kidney might cause a rotation of the renal artery on a fixed axis resulting in a twist which would cause an obstruction to the renal blood flow, recommendation was made by the urologist that the left ureter should be dilated periodically. The torsion of the right kidney, it was suggested, might be prevented by using a kidney belt or corset, which should be applied while the patient was in bed.

With the application of the corset, the patient was decidedly benefited, and three weeks later the patient asked permission to make an automobile trip back East. Since then the blood pressure has stayed fairly close to normal except for an occasional upset. Once when the patient removed the belt for a day the symptoms recurred with a blood pressure of 220/120. Another time when the patient fell and hurt her back her blood pressure was 200/100.

On Oct. 23, 1941 the patient said she was feeling well; once in a while a severe headache occurred and then her pressure would go up a little. It descended to 154. She reported that she tried taking the belt off for just one day and the pressure went up to 190 immediately.

COMMENT

This case presents many problems, as hypertension occurs in the menopause and may be just temporary. The pathologic condition of the kidney has probably been present for many years and it may have been exacerbated by the climacteric. Regardless, the pressure of the belt can be said to have forced the rotated kidney into place, thereby renewing the normal status of the renal blood flow. The only experimental observation was incidental when the patient removed her belt or fell, resulting in a rise in blood pressure.

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Special Article

HANDBOOK OF NUTRITION: III

ROLE OF FAT IN THE DIET

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These special articles on foods and nutrition have been prepared under the auspices of the Council on Foods and Nutrition. The opinions expressed are those of the authors and do not necessarily reflect the opinion of the Council. These articles will be published later as a Handbook of Nutrition.—ED.

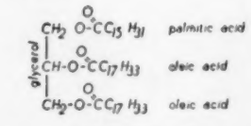
Fat is used biologically mainly as a source of energy and as a constituent of the body tissues. It has minor functions, such as carrying important accessory substances. Weight for weight, fat supplies about twice the energy of the other staple organic foods, carbohydrate and protein. It is an essential in the structure and functions of all tissues and especially of the brain and nerves. The natural fats contain many of the vitamins which are necessary for the growth, maintenance and well-being of animals and probably plants as well. Fats serve passively as heat insulation under the skin, as padding to keep the bodily organs and blood vessels and nerves in place, and for rounding out the angular contours of the bodily structure. They constitute the most important form of stored energy for tiding the animal over through periods of food scarcity and for transmitting to the offspring, as milk or egg, food material to serve until the young animal can forage for itself. Most fats are readily synthesized by animals from other foods but there are certain important exceptions, fatty acids, which must be supplied in the food and the lack of which produces the fat deficiency disease. Fat is thus an important source of energy both immediate and remote. As ordinarily used, mixed with considerable other food, it is completely and easily digested and used. When used alone or when it is the main food constituent of the diet, it is less well used and may cause important disturbances in the organism.

The proper understanding of the part taken by fat in the life processes of animals requires a consideration of the chemical nature of fat and its various related substances and the changes which they undergo in their use by animals. The characteristic constituents of the group comprising the food and body fats and related substances (ordinarily grouped under the name of lipids) are the fatty acids. These are monobasic straight chain acids, two to twenty-four or more carbon atoms in length, some of them with from one to six unconjugated double bonds per molecule. The commonest ones in both food fat and body stores are palmitic ($C_{16}H_{32}O_2$), oleic ($C_{18}H_{34}O_2$) and stearic ($C_{18}H_{36}O_2$) acids with linolic ($C_{18}H_{32}O_2$) and palmitoleic ($C_{16}H_{30}O_2$) close seconds and a variety of others mostly confined to some tissue or fluid in the organism. Some of these are butyric ($C_4H_8O_2$) found in milk fat, arachidonic ($C_{20}H_{32}O_2$) in brain, liver, muscle and other tissues, lignoceric ($C_{24}H_{48}O_2$) in brain and nerve, and cerebronic ($C_{24}H_{48}O_3$), α-hydroxylignoceric,[1] in brain. For the complete list and for other detailed information regarding classification of the fatty acids and their compounds, the reader is referred to the numerous good textbooks of biochemistry.

Melting points of the fatty acids depend on the length of chain and on the number of double bonds. The longer the chain the higher the melting point, while double bonds lower the melting point. Thus stearic acid ($C_{18}H_{36}O_2$), a long chain saturated acid, has a melting point of 69.5 C., while lauric acid ($C_{12}H_{24}O_2$) melts at 43.6 C. and oleic acid ($C_{18}H_{34}O_2$), corresponding to stearic acid but with one double bond, has a melting point of 14 C., the double bond lowering the melting point about 55 degrees C. Since the melting points of the constituent fatty acids determine the melting points of the fats and since the stored fat must be kept fluid while the animal is alive, there is often a careful adjustment of the fatty acid mixture in the fat stores.

The fatty acids exist in various types of combination in the animal body. Most common of these is that of the fats, also called neutral fats, which are triglycerides of the fatty acids. These are compounds in which the trihydroxy alcohol glycerin is combined in ester combination with three fatty acids. In nature these three fatty acids are rarely the same. Often three different fatty acids are found and in general (Hilditch's rule) [2] there will be as great a variety of fatty acids in the triglyceride molecule as are available to the animal at the time the fat was synthesized. The selection is also controlled by the necessity of a balance between saturated and unsaturated acids or perhaps by the requirement that the completed triglyceride have a melting point not far from the body temperature of the animal. The fact that these esters as well as the fatty acids themselves generally have two and sometimes more melting points some distance apart and that they can be kept in a greatly supercooled condition for long periods of time are facts which require something more complicated than the simple triester type of formula. Evidence points to the occurrence of these esters in several polymorphic forms.[3]

The formula for a typical fat unit is



Typical fat unit

which would be called palmitodiolein. The naturally occurring fats generally contain several varieties of such units.

In all living organisms fatty acids occur in several types of combination in addition to that in the fats, and, since these compounds are now believed to be either stages in the progress of the fats through the processes of metabolism or important constituents of the living cells, it is necessary to include them in the discussion. These compounds include the phosphorylated fats or phospholipids, found everywhere in animal tissues, the cerebrosides, which contain a sugar in fatty acid combination, found in the brain and nerves, and cholesterol, which always occurs along with the fats, generally free but sometimes in ester combination with the fatty acids, as in the cholesterol esters of blood plasma.

From the Department of Biochemistry and Pharmacology, University of Rochester School of Medicine and Dentistry.

1. Klenk, E.: Ueber die Cerebronsäure, Ztschr. f. physiol. Chem. **179**: 312 (Dec.) 1928.

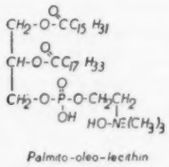
2. Longenecker, H. E.: Composition and Structural Characteristics of Glycerides in Relation to Classification and Environment, Chem. Rev. **29**: 201 (Oct.) 1941.

3. Grüntzig, W.: Ueber die Schmelzpunktsalternation der höheren, einsäurigen Triglyzeride, Ztschr. f. anorg. Chem. **240**: 313 (March 7) 1939.

PHOSPHOLIPIDS

The phospholipids or phosphorylated fats call for an extended discussion, since they are connected with the fatty acids in several stages of their metabolism and are important cellular constituents. Phosphoric acid has long been recognized as one of the necessary food constituents of both plants and animals, but only recently has light been thrown on just why it is so necessary. Thus the part which it takes in the metabolism of the carbohydrates has been well worked out, and, although the picture is incomplete in some details, enough has been shown to indicate that the phosphoric acid takes part in most of the stages of carbohydrate metabolism. In fat metabolism only the first stages of phosphoric participation are known. There are three main types of phosphorylated fats, the first two, lecithin and cephalin, being very similar in composition while the third one, sphingomyelin, is quite different. Since different fatty acids enter into each of these compounds, there are several members of each group.

Lecithin is believed to have a composition represented by the formula

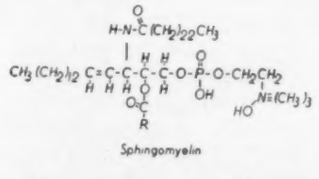


Palmito-oleo-lecithin

This would be called palmito-oleo-lecithin. As may be seen, it is an ordinary fat with one of the fatty acids on the glycerin molecule replaced by phosphoric acid in combination with the base choline.

Cephalin is believed to differ from lecithin only in the nature of the base in combination with the phosphoric acid, which in this case is either aminoethyl alcohol ($CH_2OH.CH_2.NH_2$) or its carboxylated form, serine. There are two forms of both lecithin and cephalin, the α form in which the phosphoric group is on the terminal carbon of the glycerin and the β form in which it is on the middle carbon. Both forms occur in tissues, and it is significant that α-lecithin and β-cephalin disappear during starvation, while the β-lecithin and α-cephalin persist.[4]

The third phospholipid, sphingomyelin, as the derivation of the name indicates, is still the "mystery" substance. It is found mainly in brain and nerve and in small amounts in other tissues including the blood. The present accepted formula is



Sphingomyelin

It would be called lignoceryl-sphingosine-phosphoric-acid-choline-ester. It is made up of the two bases sphingosine, which is an unsaturated C_{18} chain with one amino and two hydroxy groups, and choline, both of which are united to the phosphoric acid by ester linkages. It contains one fatty acid, ordinarily the saturated lignoceric ($C_{24}H_{48}O_2$), united with the sphingosine as an acid amide, and often another fatty acid united by an ester linkage with the other hydroxyl group. The fact that sphingomyelin sometimes contains two fatty acids and sometimes only one [5] indicates that it may be of importance in the transport of fatty acids. The fact that the fatty acid in ester linkage may be detached by alkaline hydrolysis or by lipases, while the amide linked fatty acid is not affected, is of unknown significance. Fragments of sphingomyelin, e. g. lignoceryl sphingosine, were found by Thudichum in brain and later by others in liver,[6] and sphingosine phosphoric acid choline has been reported in kidney.

A significant difference between the phospholipids and the fats is that the phospholipids contain groups which have a strong affinity for water (phosphoric acid and bases) which render the phospholipids miscible with if not actually soluble in water. The phospholipids thereby provide a physical link between the water insoluble fats and cholesterol on the one hand and the tissues and fluids of the animal body which are either water soluble or mix readily with water. Phospholipids and cholesterol are found in cell walls and membranes and, because they are intermediate in properties between the water insoluble fats and the watery environment, undoubtedly serve to regulate the passage of water and water soluble material as well as to facilitate the passage of fat in and out of such cells as those of the intestinal epithelium, the liver cells and the cells of the fat stores. In the intestine this passage appears to be brought about by processes of hydrolysis and resynthesis in which the phospholipids take part, and the same may be true in the case of other cells. One of the impressive phenomena of cellular processes in general is the ease with which hydrolysis and recombination take place. Lecithin and sphingomyelin are nearly neutral substances, for although they contain strong acidic and basic groups these appear to be internally compensated either by union of the opposing groups with loss of water or by the zwitterion form. Cephalin, on the other hand, may be titrated as a monobasic acid, since the bases which it contains, aminoethyl alcohol or serine, are too weak to interfere with the titration of the strongly acidic third hydrogen of the phosphoric acid. Its acidic character gives it the power to combine with the basic groups of proteins and with metals, a fact which may explain its importance in such processes as blood coagulation. The fact that cephalin sometimes contains serine and sometimes the decarboxylated base (aminoethyl alcohol) may explain the fact that when it is too highly purified it is no longer effective in blood coagulation.

Lecithin and cephalin exist in living organisms almost entirely in the "complete" form, i. e., have their full complement of fatty acids and base. Under certain circumstances they may lose one fatty acid, becoming lysolecithins and lysocephalins, or they may lose the base, becoming phosphatidic acids. Lysolecithin and lysocephalin are highly dangerous substances because, as their names indicate, they bring about extensive lysis and destruction not only of red blood cells but of tissue cells as well. The increased affinity for water which the loss of one fatty acid confers makes them excellent wetting agents with the result that, entering the cell wall, they upset the water balance between cell and fluid, causing swelling and bursting of the cells. Much of the destructive power of some snake venoms is due

4. MacLachlan, P. L.; Hodge, H. C.; Bloor, W. R.; Welch, E. A.; Truax, F. L., and Taylor, J. D.: Lipids of the Fasting Mouse: II. The Fat to Water Relation and the Fractionation of the Liver Phospholipids, J. Biol. Chem. **143:** 473 (Apr.) 1942.

5. Reichel, M., and Thannhauser, S. J.: Studies on Animal Lipids: XVII. The Synthesis of Lignocerylsphingosine Fatty Acid Esters (Sphingosine Fats) and Sphingosine Amides (Ceramides), J. Biol. Chem. **135:** 15 (Aug.) 1940.

6. Thannhauser, S. J., and Fränkel, E.: Ueber das Lignoceryl-sphingosine: II. Zur Kenntnis des sogenannten Unverseifbaren der Säugetierleber, Ztschr. f. physiol. Chem. **203:** 183, 1931.

to the fact that they contain an enzyme which produces these lyso compounds. Phosphatidic acid is not known to occur in animals but is found in plant leaves.[7]

Sphingomyelin may take on an extra fatty acid in ester combination at its second hydroxyl group[8] and, since this acid has been found to be one of the common fatty acids (palmitic), it seems likely that sphingomyelin takes a more active part than has been supposed in the processes of fat metabolism.

Lecithin and cephalin in the living organism appear to be very labile substances, exchanging their fatty acids and their phosphoric acid with similar materials coming in with the food. The exchange of fatty acids takes place rapidly in the intestinal epithelium; in fact, it appears that this passage of fatty acids into and out of the framework of the epithelial phospholipids is the method or an important method of fatty acid absorption. Phosphoric acid of the food also has been shown to exchange with the phosphoric acid of the cellular phospholipid. These exchanges have been satisfactorily demonstrated by the modern use of labeled or tagged fatty acids and phosphorus as food. The fatty acids used were those of cod liver oil and elaidin by Sinclair,[9] the latter prepared by treatment of ordinary olive oil with nitrous acid. The phosphorus used was the P^{32} isotope, which is radioactive and has been used as a tracer substance in fat metabolism by several investigators, notably Chaikoff and his associates,[10] and in this laboratory by Haven.[11] Other labeled fatty acids which are satisfactory are those containing conjugated double bonds, either natural as in tung oil or artificial as produced by prolonged saponification of corn oil. These have been used by Burr and his associates.[12]

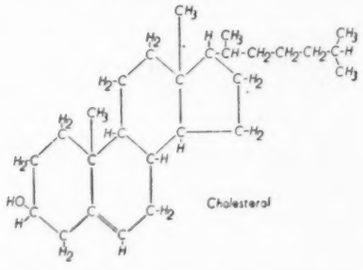
Rapid exchanges were found also in the lipids of liver in the case of both fatty acids and phosphoric acid and considerably less rapid in muscle and most other tissues. Brain, nerve tissue and testicle have a very slow exchange. The significance of these exchanges in the tissues is not yet understood, but they emphasize the fact that the fatty acid compounds in tissues are quite labile, giving up or taking on new units according to the supply from the food. This conception of ever labile compounds has been found to hold also for the body proteins[13] and is compatible with the fact that chemical processes in the animal body must be carried on without the usual laboratory aids in bringing about chemical changes, i. e., heat, strong acids, bases or other strong reagents. The warm blooded animal body is a well regulated thermostat kept at about 37 C. and likely to be severely damaged by temperatures much below and especially much above that "normal" level. The body fluids are very nearly neutral in reaction and are similarly regulated about the neutral point. Close regulation extends also to concentration of the various bodily constituents and to the balance between fluids inside and outside the cell. Consequently the body components must be such as can undergo fundamental transformations readily under narrowly limited conditions.

Although free exchange has been established of the various constituents of the phospholipids (at least of lecithin and cephalin) with the incoming ones from the food, certain preferences have been established. Thus Sinclair[14] found that, although the fatty acid constituents of the phospholipids of the intestinal mucosa, liver and muscles changed in response to the fatty acids of the food, the more highly unsaturated fatty acids of cod liver oil were taken up more rapidly and retained more tenaciously than other fatty acids. The special desirability of highly unsaturated acids as phospholipid constituents fits in with other findings regarding the tissue phospholipids—their ready oxidizability in air and hence the difficulty of preparing them in even approximately pure form.

The need of the organism for the more highly unsaturated fatty acids finds expression in the fat deficiency disease which develops in experimental animals as the result of the lack of certain necessary fatty acids in the diet[15] and is cured by the addition to the diet of these acids or acids from which the essential ones can be made. MacLean and her associates[16] have suggested that the essential unsaturated acid is arachidonic ($C_{20}H_{32}O_2$), a four double bond acid which the organism can manufacture from those acids, linoleic and linolenic, which cure the fat deficiency disease.

CHOLESTEROL AND CHOLESTEROL ESTERS

Cholesterol ($C_{27}H_{45}OH$) has the formula shown.



It is a member of the large group known as sterols and is part of a still larger group known as the steroids or sterids. Also members of this group and chemically closely related to cholesterol are the bile acids, the sex hormones and substances occurring as glucosides in such compounds as digitalis and toad poisons. Whether cholesterol can be changed into these important substances or has any physiologic relation to them has not been shown. Cholesterol is connected with the fats in their role in the animal organism because it always occurs along with them and combines with the fatty acids to form the cholesterol esters. The cholesterol esters occur normally in notable amounts only in blood plasma and the adrenal cortex, but in abnormal

7. Channon, H. J., and Chibnall, A. C.: The Ether Soluble Substances of Cabbage Leaf Cytoplasm: IV. Further Observations on Diglyceridephosphoric Acid, Biochem. J. **21:** 1112, 1927.

8. Thannhauser, S. J., and Reichel, M.: Studies on Animal Lipids: XVI. The Occurrence of Sphingomyelin as a Mixture of Sphingomyelin, Fatty Acid Ester and Free Sphingomyelin, Demonstrated by Enzymatic Hydrolysis and Mild Saponification, J. Biol. Chem. **135:** 1 (Aug.) 1940.

9. Sinclair, R. G.: The Metabolism of the Phospholipids: VIII. The Passage of Elaidic Acid into Tissue Phospholipids: Evidence of the Intermediary Role of Liver Phospholipid in Fat Metabolism, J. Biol. Chem. **111:** 515 (Oct.) 1935.

10. Perlman, I.; Ruben, S., and Chaikoff, I. L.: Radioactive Phosphorus as an Indicator of Phospholipid Metabolism: I. The Rate of Formation and Destruction of Phospholipids in the Fasting Rat, J. Biol. Chem. **122:** 169 (Dec.) 1937.

11. Haven, F. L.: The Rate of Turnover of the Lecithins and Cephalins of Carcinosarcoma 256 as Measured by Radioactive Phosphorus, J. Nat. Cancer Inst. **1:** 205 (Oct.) 1940.

12. Barnes, R. H.; Miller, E. S., and Burr, G. O.: The Absorption and Transport of Fatty Acids Across the Intestinal Mucosa, J. Biol. Chem. **140:** 233 (July) 1941.

13. Schoenheimer, Rudolf; Ratner, S., and Rittenberg, D.: Studies in Protein Metabolism: X. The Metabolic Activity of Body Proteins Investigated with *l*(—)-Leucine Containing Two Isotopes, J. Biol. Chem. **130:** 703 (Oct.) 1939.

14. Sinclair, R. G.: The Metabolism of the Phospholipids: V. The Relationship Between the Amount of Fat Ingested and the Degree of Unsaturation of the Phospholipids and Neutral Fat in the Tissues of the Rat, J. Biol. Chem. **96:** 103 (April) 1932.

15. Burr, G. O., and Burr, Mildred M.: A New Deficiency Disease Produced by the Rigid Exclusion of Fat from the Diet, J. Biol. Chem. **82:** 345 (May) 1929.

16. Hume, Eleanor M.; Nunn, L. C. A.; Smedley-MacLean, Ida, and Smith, Hannah H.: Fat Deficiency Disease of Rats. The Relative Curative Potencies of Methyl Linoleate and Methyl Arachidonate with a Note on the Action of the Methyl Esters of Fatty Acids from Cod Liver Oil, Biochem. J. **34:** 879 (June) 1940.

conditions they are found in deposits in various parts of the animal body—in the liver, in fatty livers especially when caused by cholesterol feedings, in the walls of diseased arteries either as mushy deposits (atherosclerosis) or in the actually hardened arteries [17] and in gallstones. Cholesterol and cholesterol esters are among the lipids present in the deposits of Niemann-Pick and Schüller-Christian diseases and in the blood and skin and joint nodules of essential hypercholesterolemia. Whether the cholesterol esters of these deposits represent normal stages in the metabolism of the fats or whether they represent a mechanism for the disposal of cholesterol or unusable fatty acids remains unsettled.

The fact that the cholesterol esters of the blood plasma constitute from 60 to 70 per cent of the total plasma cholesterol and the fact that the cholesterol absorbed through the intestine is esterified with the absorbed fatty acids to about the same extent [18] indicate that it is concerned with the transport if not the metabolism of the fatty acids. Recent work [19] as well as older work [20] indicates that the fatty acids in combination with the cholesterol are relatively highly unsaturated (average about two double bonds) which leads to the belief that the cholesterol combination has to do mainly with the more unsaturated acids. The presence of cholesterol esterases in blood and tissues is the basis for Sperry and Stoyanoff's [21] conception that, since cholesterol esters exist in the blood but not in normal tissues, these enzymes are responsible both for the cholesterol-cholesterol ester equilibrium in the blood and also for the breaking up of the ester in its passage into the tissues.

Animals vary a good deal in their ability to absorb and metabolize cholesterol. Herbivorous animals such as the rabbit absorb it slowly and, having absorbed it, have difficulty in disposing of it. In these animals it raises the blood cholesterol and is deposited in characteristic fashion in arterial walls and other places. In omnivorous or carnivorous animals such as the human being and the dog, moderate feeding of cholesterol has no effect on the blood cholesterol nor has it been shown to have any effect on the arterial walls. Gallstone formation has also been shown to be independent of the cholesterol level in the diet. The reason for the lack of effect of dietary cholesterol in omnivorous and carnivorous animals lies in their ability to excrete the excess by way of the intestine. Animals can oxidize cholesterol but slowly. Normally the excretory mechanism is adequate to keep the body in balance as regards cholesterol, but under some circumstances it can be overloaded, with the result that the level of blood cholesterol rises. It has been shown that animals can manufacture cholesterol as needed from compounds of relatively small molecular size.[22]

Cholesterol is confined to the animal kingdom. In plants and bacteria there are other but closely related sterols which presumably have a similar function in their life processes. All available evidence indicates that animals cannot use these sterols in place of cholesterol, in fact cannot absorb them from the alimentary tract.

With the exception of the adrenals the cholesterol is normally present in the cells and tissues almost entirely in the free form, while in the blood plasma it is about two-thirds combined with fatty acids as esters. Various figures are available regarding the content of cholesterol in normal human blood, the differences being due to a number of causes. Differences in analytic method will explain some of the divergence: for example digitonin precipitation method always gives lower results than the colorimetric method based on the Liebermann-Burchard reaction. Since even the digitonin method is not specific for cholesterol, it seems likely that true cholesterol values have not yet been found. The relative values reported are, however, probably as useful for most purposes as absolute values.

Diet undoubtedly plays a considerable role in blood cholesterol values, especially in herbivorous animals, although moderate effects are demonstrable in omnivorous and carnivorous animals as well.

The thyroid secretion appears to have an effect on the blood cholesterol level. Hyperthyroidism lowers blood cholesterol as though the more intense metabolism in this condition resulted in a more complete combustion, while in hypothyroidism the blood cholesterol level is higher. Since all workers have not obtained pronounced differences, the thyroid effect should be regarded as probable but not invariable.

In the variety of nephritis commonly called nephrosis, the blood cholesterol values may reach very high levels, five or six times the normal, and are accompanied by fatty (cholesterol ester) deposits in the kidneys. The reason for the high values is unknown.

In diabetes before the insulin era cholesterol and fat values in the blood were often very high, but with insulin treatment and inclusion of carbohydrate in the diet these high values are exceptional. The earlier values were undoubtedly due to the unbalanced, excessively high fat diet.

Essential hypercholesterolemia in human beings appears to be analogous to the state of affairs found in normal rabbits—a very low ability to destroy or excrete cholesterol. The result is that the cholesterol of animal food accumulates in the blood, resulting in excessive values and in depositions of cholesterol similar to the tophi of gout in various places in the body such as the joints and tendons. The symptoms are relieved by giving the patient a vegetable diet (plant sterols not being absorbed), but the disappearance of cholesterol from the nodules is a very slow process.

Cholesterol, mostly in the free form, is found in all bodily tissues, being especially abundant in the adrenals (1.5 per cent, mostly as ester), brain (1 to 1.5 per cent, all free), liver (0.3 per cent) and blood (about 0.2 per cent, two thirds as ester). The cholesterol content of muscle varies with the type of muscle, with the species and with activity. Smooth muscle has the highest content (0.18 to 0.2 per cent moist weight), ventricle muscle (0.14 to 0.2 per cent moist weight) and skeletal (0.07 to 0.09 per cent moist weight).

Hen's egg yolk contains about 1.5 per cent of cholesterol, which would amount to about 0.3 Gm. per egg. Milk contains about 0.02 per cent, amounting to about 0.2 Gm. per quart.

The human being loses by the feces about 1 Gm. of sterol daily, most of which arises in the food either

17. Schönheimer, R.: Zur Chemie der gesunden und der atherosklerotischen Aorta: I. Ueber die quantitativen Verhältnisse des Cholesterins und der Cholesterinester, Ztschr. f. physiol. Chem. **160:** 61 (Oct.) 1926.
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21. Sperry, W. M., and Stoyanoff, V. A.: The Enzymatic Synthesis and Hydrolysis of Cholesterol Esters in Blood Serum, J. Biol. Chem. **126:** 77 (Nov.) 1938.
22. Schoenheimer, R., and Breusch, F.: Synthesis and Destruction of Cholesterol in the Organism, J. Biol. Chem. **103:** 439 (Dec.) 1933.

as cholesterol in animal food or as unabsorbed sterols in the vegetable part of the diet.

In most body tissues and fluids there is a well defined balance or ratio between the phospholipid and cholesterol. This ratio varies for different tissues but is fairly constant and characteristic for a single tissue.

In the accompanying table the phospholipid content and the phospholipid/cholesterol ratios are arranged in the order of magnitude: As may be seen, there is almost a reversal in the relative position of the brain and the muscle in the two columns of the table. Brain, which has the highest phospholipid, has the lowest phospholipid/cholesterol ratio, owing to its high cholesterol content, while voluntary muscle, which has the lowest phospholipid content, has nearly the highest phospholipid/cholesterol ratio, owing to its still lower cholesterol content. The position of the other items in the table is practically the same in the two columns. Among the muscles the ratios for skeletal muscle and heart are the same (14 to 16), while for smooth muscle the ratio is 4, owing to the much higher content of cholesterol, the phospholipid value being about the same as in skeletal muscle. The high cholesterol is thought to be related to the automatic character of the muscle. Smooth muscle contracts regularly independently of

Phospholipid/Cholesterol Ratios

Phospholipid Content % Moist Weight		Phospholipid/Cholesterol Ratio	
Brain	4.0	Liver	18
Liver	3.0	Voluntary muscle	16
Heart	1.8	Heart	16
Kidney	1.4	Kidney	11
Lung	1.2	Lung	6
Serum	0.2	Serum	2.5
Voluntary muscle	0.5-1.0	Brain	2.5

external nervous stimuli. Heart muscle also contracts automatically and has a high cholesterol content, but in this case the high cholesterol is balanced by a correspondingly high phospholipid content, so that the ratio remains high. Since nervous tissue is present in muscle and contains both phospholipid and cholesterol, it would be desirable to know the extent of its contribution to the phospholipid and cholesterol of the muscle. Up to the present, no means for such a study has been available. There may be some significance in the fact that in smooth muscle, which is spontaneously active, there is nearly the same phospholipid/cholesterol ratio as in brain.

It may be noted here that creatine phosphorus (phosphocreatine) and lipid phosphorus (phospholipid) appear to be in inverse relationship in heart and skeletal muscle. Creatin phosphorus in heart is about 6 mg. per hundred grams with lipid phosphorus about 80 mg. per hundred grams, while in skeletal muscle the creatine phosphorus is about 60 mg. per hundred grams and the lipid phosphorus about 30 mg. per hundred grams. As is well known, the phosphocreatine of heart muscle must be promptly renewed if the muscle is to continue active, while skeletal muscle can work for a relatively long time before its phosphocreatine is exhausted. A relation between the high phospholipid content of heart muscle and its low phosphocreatine seems likely, and it is a reasonable assumption that the phospholipid is a readily available source of energy for the renewal of the phosphocreatine and perhaps of supply of phosphorus for the compound.

FAT METABOLISM

An understanding of the way in which fat is dealt with in the body is necessary for determining its function in the animal economy. The animal body is about three-fourths water, and practically all reactions which go on in life take place in water solution or in the presence of water. Solubility or miscibility in water is a basic requirement for utilization. Fat and its main constituent, the fatty acids, are insoluble in water, and various devices are employed to make them useful in the watery environment.

The fat entering the organism as food is, like all other foods, first broken up into its constituent parts, the fatty acids and glycerol. This process, hydrolysis, is brought about by enzymes (lipases) supplied mainly in the pancreatic juice. The lipases are in water solution and, since water does not penetrate fat, the action can take place only at the surface of the fat particles. It would therefore be slow. The devices employed to bring the splitting time within the limits allowed for digestion (about four hours) are first to increase greatly the surface, which is done by emulsification. Emulsification is accomplished by the help of a small amount of soap formed by interaction of the alkali of the pancreatic secretion with free fatty acid always present in fat. The soap together with other emulsifying agents, phospholipid (present in the pancreatic juice and the bile) and the bile salts, rapidly break up the masses of fat into minute particles, greatly increasing the surface presented to lipase action. Splitting proceeds rapidly and is speeded up by the prompt removal of the split products by absorption. In the absorption the bile salts are especially useful. The exact mode of action of these substances is not known, but several factors enter and are important. First, they form water soluble, diffusible compounds with the fatty acids. Second, they are excellent wetting agents and penetrate easily into the complicated absorbing surface. They have an affinity both for fatty acids and the watery absorbing surfaces and in this way carry the water insoluble fatty acids into close contact with and eventually through the walls of the epithelial cells. The water soluble form necessary for the absorption of the fatty acids is thus provided by the bile salt combination. Another water soluble form of the fatty acid is its sodium salt called soap. The importance of soaps in fat absorption has been a matter of dispute for many years and is now recognized as secondary. The reaction of the intestinal contents is generally slightly on the acid side of neutrality and, under these circumstances, soap if formed would soon be broken up again. Also it has been found that soap in any considerable concentration is irritating and destructive to the intestine. It is apparently useful in the first stages of fat metabolism, emulsion formation and hydrolysis, after which the bile salts become the major agent in absorption.

During its stay in the epithelial cells the absorbed fatty acid is recombined into fat before being passed out of the cells into the collecting system, which in the case of the fats is the lymph. A number of factors appear to be involved in this resynthesis. Sinclair [23] showed by the use of fats of pronounced characteristics, coconut and cod liver oils, that the phospholipids of the epithelium were involved, since the newly absorbed fatty acids were found in the epithelial phospholipid in amounts sufficient to indicate that most or all of

23. Sinclair, R. G.: The Role of the Phospholipids of the Intestinal Mucosa in Fat Absorption, with Additional Data on the Phospholipids of the Liver and Smooth and Skeletal Muscle, J. Biol. Chem. **82**: 117 (April) 1929.

the absorbed fatty acids passed into the framework of the intestinal phospholipids. These therefore constitute a stage in the absorption process. The resynthesized fat appearing in the thoracic duct is generally not the same as the absorbed fat but differs from it in degree of unsaturation, melting point and mean molecular weight of the fatty acids. These differences seem to mean either that the degree of unsaturation is adjusted (up or down) in the epithelium or that there is a mixing of the absorbed fat with fat brought from nearby depots. There appears to be an attempt to adjust the melting point of the incoming fat to a point near to body temperature, since high melting fat when fed appears in the chyle with a considerably lower melting point, and low melting fat has its melting point adjusted upward.[24] That there is a dilution of absorbed fat with body fat appears probable from recent work.[25] As to the fate of the absorbed fat, the belief has always been that it passes into the lymph system and enters the blood stream as fat via the thoracic duct. All efforts to demonstrate other paths of absorption, e. g. the blood stream via the portal system, have so far been unsuccessful. On the other hand, it has never been demonstrated that all the absorbed fat passes into the blood by way of the thoracic duct; in fact, recent attempts to recover absorbed fat from the thoracic duct have given remarkably small returns.[25] As noted earlier in the discussion, fat is believed to be hydrolyzed and then absorbed as fatty acid and glycerol, but the possibility of absorption in the unhydrolyzed state has never been entirely eliminated. Furthermore, the manner of passage of the resynthesized fat out of the epithelial cells and into the lacteals of the villi is not known nor is the method of passage out of the blood into the storage and tissue cells any better understood. The best explanation of the latter two processes, and of the absorption of unsplit fat if any is absorbed, is that the fat passes the cell membrane by solution in it, as in the case of water soluble molecules, the phospholipid of the membrane aiding in the process.

A considerable portion of the absorbed fat appears promptly in the liver, which is for fat, as it is for other foods, a place of temporary storage for excess food which would otherwise flood the organism and probably be wasted either by unnecessary combustion or by excretion. Of the fat thus mobilized to the liver a considerable portion, perhaps all of it, is changed to phospholipid and then probably a large percentage is discharged into the blood and distributed to other tissues. The change of fat to phospholipid in the liver appears to be a necessary step for its later use. If formation of phospholipid is prevented there is an accumulation of fat, which in extreme instances may amount to half the liver weight and which eventually leads to death as the result of interference with normal liver function. The main cause of the fat accumulation has been shown to be a lack of the base choline, a necessary constituent of lecithin, since the fatty liver may be prevented and cured by the administration of choline. When choline or its "makings" are lacking, lecithin cannot be formed and the fat accumulates. The story is not quite as simple as that because of the involvement of other factors. For example, there is always some cholesterol ester present in the accumulated fat, and the amount is larger when there is much cholesterol in the diet. The formation of cholesterol esters with the fatty acids and their storage appears to be one of the means used by the organism for disposing of excess cholesterol as well as excess of certain fatty acids, especially the more highly unsaturated ones.[26] The accumulation of cholesterol esters is always more difficult to clear out of the liver than the fat. Instead of choline, substances which supply the material for making choline are effective in curing the fatty liver. Certain proteins, casein among them, are effective and the constituent of casein mainly responsible has been shown to be the amino acid methionine, of which the methyl group is the important part (there being three methyl groups in choline).

The fate of the phospholipid formed in the liver and hence the fate of the fat from which it was formed is not known. The use of tracer substances has not given clear answers, since their use has shown, along with pertinent facts, that constituents of living tissues are in a continuous state of flux. In the proteins, whole sections, single amino acids or parts of amino acids may be taken out and replaced by new ones without the chemical composition of the protein being appreciably changed.[13] Similarly, in the case of the phospholipids, the phosphorus and the fatty acids have been shown to be replaceable by similar substances in the food. Probably choline and glycerin are also replaceable, so that the finding of a phospholipid in muscle which has the same labeled fatty acid or phosphorus which was found earlier in the liver need not mean that the liver phospholipid has been transferred to the muscle, although it may have been.

A second function of the liver in fatty acid metabolism which has been recently shown to be important and perhaps essential is its ability to break the long carbon chains of the fatty acids into four carbon fragments which appear sometimes as acetoacetic acid ($CH_3.CO.CH_2.COOH$), sometimes as beta-hydroxybutyric acid ($CH_3.CHOH.CH_2.COOH$) and sometimes as acetone ($CH_3.COCH_3$). These substances, known as acetone bodies or ketone bodies, have been known for a long time but have been regarded as dangerous by-products in fatty acid metabolism, dangerous because they are fairly strong acids and use up significant amounts of the metallic bases of the body for their neutralization and excretion. They appear in the blood and urine of human beings and some other animals when a large proportion of the energy is supplied by fat, as in starvation or in untreated diabetes mellitus. They were considered to be the partially oxidized last four carbon atoms in the fatty acid chain, which were what was left after successive β oxidation and which for some unexplained reason were unoxidizable unless carbohydrate was being burned at the same time ("fats can burn only in the fire of the carbohydrates"). Work in the last ten years (summarized by Stadie and his associates[27]) has shown (*a*) that these substances are normally formed from fat in large amounts by the liver and to a considerable extent by the kidney, more than ten times the amount which appears in the urine, (*b*) that they are burned by muscle and other tissues, which however cannot form them, and (*c*) that they may supply most of the energy needed by the heart and presumably other tissues. The demonstration that these ketone acids can be formed and used by normal tissues in amounts large enough to

24. Bloor, W. R.: On Fat Absorption: III. Changes in Fat During Absorption, J. Biol. Chem. **16**: 517, 1913-1914.
25. Little, J. M., and Robinson, C. S.: The Transportation of Absorbed Lipids, Am. J. Physiol. **134**: 773 (Nov.) 1941.
26. Kelsey and Longenecker,[10] Bloor.[20]
27. Stadie, W. C.; Zapp, J. A., Jr., and Lukens, F. D. W.: The Effect of Insulin on the Ketone Metabolism of Normal and Diabetic Cats, J. Biol. Chem. **132**: 423 (Jan.) 1940.

account for the total amount of fat metabolized puts an entirely new face on their importance and use in the organism, raising them from the status of harmful and occasional accidents to that of regular stages in fatty acid breakdown.

In many ways these substances are analogous to lactic acid which appears in carbohydrate breakdown. They appear in excess in blood and urine whenever unusual pressure is put on the organism to burn fat, just as lactic acid appears in excessive amounts in blood, urine and sweat when unusual pressure is put on the carbohydrate burning mechanism, as in heavy muscular work. They are relatively strong acids, call for neutralization to about the same extent, and have the same or only slightly greater potential menace to the state of neutrality in the organism as lactic acid. In their formation from fatty acids there is considerable energy loss just as there is in the change from glycogen or *d*-glucose to lactic acid. The loss is probably much greater in the case of the ketone acids because it is due to oxidation while the diminished energy value of lactic acid is due to internal rearrangement in the breaking of the glucose molecule. The liberation of energy in the change from glycogen to lactic acid is put to good use in bringing about the recovery of the contraction mechanism of the muscle. No consideration has as yet been given to the much greater liberation of energy in the change from a C_{16} fatty acid to four 4 carbon ketone acids, but there is little doubt that it could be and probably is put to similar uses. In the changes involved in the formation of lactic acid from glycogen or *d*-glucose, phosphoric acid figures largely. The participation of phosphoric acid in the metabolism of the fatty acids has not been demonstrated beyond the first stage, that of phospholipid formation from fat, but it seems probable that much if not all of the metabolized fat does go through the phospholipid stage. As has already been noted, not much is known about the fate of the phospholipid formed in the liver, but since the ketone body acids are also formed there the obvious next step would be the formation of ketone acids from the fatty acids of the phospholipid and, if the analogy with lactic acid holds, they are formed by way of intermediate phosphorylated compounds. Nothing has yet been done to elucidate these later stages of fatty acid metabolism.

NUTRITIONAL VALUE OF FATS

Very little need be said about the relative nutritional value of fats and hence of availability and distribution for the reason that most of the ordinary food fats of both plant and animal origin consist mainly of the same few fatty acids—oleic, palmitic and stearic—in varying proportions, and it is to be expected that they would not differ much in digestibility or in metabolic usefulness. This is found in general to be the fact.[28] When the melting point is high, digestion is slower and there is a tendency for unabsorbed fat to appear in the feces. The rate of absorption of various fats was found by one group of investigators[29] to be in the following order: linseed (best), then olive, whale, soybean, peanut, lard (rancid), cottonseed, cocoa butter, coconut and palm, but all were well utilized. Fats with a melting point above 37.8 C. were slowly absorbed. Laxative effects were noticed in only two fats of a series of sixty-three fats fed at a 50-115 Gm. level to human subjects. These were cocoa butter and goose fat.[28] At 140 Gm. a day, beef fat was laxative. Hydrogenated oils, as long as the melting point remains below 37.8 C., are as well absorbed as the natural oils.

Natural fats carry in solution a number of non-fat substances some of which, for example, the fat soluble vitamins, are useful and desirable but have little importance in the metabolism of fat as such. Other fat soluble substances such as the sterols may in some cases be useful, as for example cholesterol in animal fats, while the sterol of plant fats are not useful because they are not absorbed by animals. This fact is made use of in treating certain individuals who have difficulty in excreting cholesterol, a shift from an animal to a plant diet stopping the cholesterol inflow.

Milk fat or butter contains, in addition to the common fatty acids, oleic, palmitic and stearic, considerable amounts of short chain fatty acids from butyric (C_4) up to C_8 which are presumably especially useful to the young animal. Milk fat contains also small amounts of cholesterol and phospholipid and varying amounts of the fat soluble vitamins or their mother substances. Egg fat is especially rich in phospholipid, cholesterol and vitamins. The fatty acids in both milk fat and egg fat are not especially notable since they originate largely from the food of the mother.

Aside from those well known dietary factors or vitamins which are essential for the general well-being of the living organism, two others have been found to be essential for the proper carrying on of fat metabolism. These are choline, the lack of which causes fatty livers and eventually death through liver failure, and certain "essential" fatty acids the nature of which is not entirely established. One, and perhaps the main one of these, is arachidonic acid, although linoleic and linolenic acids are effective in curing the fat deficiency disease.[16] They appear to do so by transformation into arachidonic acid.

Since choline or its "makings" are essential for the necessary phospholipid stage in fat metabolism, materials for its synthesis must be supplied by the food. Choline itself is found in foods containing lecithin or sphingomyelin, such as brain, egg yolk, glandular products, meat, especially heart muscle and to a less extent in other animal foods. It may be synthesized by the organism. In its construction the methyl groups appear to be the critical constituents and there are not many sources of these. The most important one is the amino acid methionine, methyl homocystein or *a*-amino-*γ*-methylthiol-n-butyric acid, which readily yields its methyl group in a variety of reactions in the animal body.[30] Methionine is supplied in food proteins, and of these casein has been found to be a satisfactory source. Undoubtedly other "good" proteins or mixtures of protein would provide an adequate supply of methionine.

The essential fatty acids, especially linoleic, are widely distributed in both plant and animal fats and are found also in combination in starches, so that their supply in adequate amounts needs no special consideration. These acids are low in amount or absent in certain tropical seed fats, as for example coconut oil, which are used in making oleomargarine, and this fact has been urged as an objection to the use of oleomargarine instead of butter. However, commercial oleomargarine generally contains a considerable proportion of animal

28. Langworthy, C. F.: The Digestibility of Fats, J. Indust. & Engin. Chem. **15**: 276 (March) 1923. Holmes, A. D.: Digestibility of Fats Taken from Different Parts of the Animal Body, J. Oil & Fat Ind. **3**: 11 (Jan.) 1926.

29. Steenbock, Harry; Irwin, Margaret, H., and Weber, Janet: The Comparative Rate of Absorption of Different Fats, J. Nutrition **12**: 103 (July) 1936.

30. du Vigneaud, Vincent; Cohn, Mildred; Chandler, J. P.; Schenck, J. R., and Simmonds, Sofia: The Utilization of the Methyl Group of Methionine in the Biological Synthesis of Choline and Creatine, J. Biol. Chem. **140**: 625 (Aug.) 1941.

fat or even butter, and most diets contain enough other sources of these acids to make up for any deficiency. On the other hand, marine animal fats contain large amounts of the essential fatty acids.

As sources of the essential fatty acids may be listed brain, organs and tissues of animals which are not deficient in these acids, and several natural fats generally with a high iodine number (degree of unsaturation) such as cod liver oil, corn and cotton oil, butter and egg yolk (provided the source animals are not fat deficient). Linseed oil is rich in the necessary acids but is unpalatable unless specially treated. In fact, most of the natural oils (liquid fats) will yield enough of the required essentials if taken in ordinary amounts.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Acting Secretary.

DIGITALINE NATIVELLE. — Digitaline Cristalisée (Nativelle).—A glucosidal substance derived from the dried leaves of Digitalis purpurea, first prepared by Nativelle (*J. Pharm. Chem.* **9**:225, 1869). The empiric formula of digitaline Nativelle closely approximates $C_{41}H_{64}O_{13}$. It is standardized by the intravenous cat method of Hatcher and Brody: 0.42 mg. equals 1 cat unit, but the therapeutic dose is much less than that of digitalis in terms of cat units.

Actions and Uses.—The action of digitaline Nativelle is like that of digitalis but its cardiac action is more persistent than that of digitalis.

Dosage.—The full therapeutic effects are induced in a patient who has not had digitalis during the previous three weeks by the oral administration of a total of from 1.25 to 1.5 mg. of digitaline Nativelle given in fractional doses. This is the therapeutic equivalent of from 1.3 to 1.6 Gm. (20 to 25 grains) of digitalis. The total dose is given in fractions of from 0.25 to 0.5 mg., at intervals of from four to six hours. The total daily maintenance dose is from 0.1 to 0.2 mg. Patients may be digitalized by starting with total daily doses of 0.2 mg.; such doses usually induce the full therapeutic effects in about one week. The great potency of digitaline Nativelle requires a careful observance of the proper technic of its administration.

Poisoning with digitaline Nativelle requires no treatment except the utmost quiet in bed, with a sedative, such as phenobarbital, if necessary to secure rest. The stomach should not be washed unless there is reason to believe that it contains some of the poison, but severe and repeated vomiting is a prominent symptom of poisoning with all digitalis bodies.

Tests and Standards.—

Digitaline Nativelle appears as thin, colorless, odorless, elongated, rectangular platelike crystals, possessing a bitter taste. It is practically insoluble in water, ether and glycerin; soluble in acetone, chloroform, ethyl alcohol and pyridine. Digitaline Nativelle may sinter at 230 C. and melts finally at from 253 to 263 C.

Digitaline Nativelle dissolves in cold, concentrated hydrochloric acid to form a colorless solution, but if this solution is heated on a water bath a green color should be obtained.

Dissolve a crystal of digitaline Nativelle in 2 cc. of glacial acetic acid containing a trace of ferric chloride and layer the solution on 2 cc. of concentrated sulfuric acid: a brown color should be produced at the zone of contact of the two liquids. This color gradually changes to green and finally to indigo blue; after half an hour the entire acetic acid layer will become blue.

E. FOUGERA AND COMPANY.

Digitaline Nativelle (crystals): bulk.

Tablets Digitaline Nativelle: 0.1 mg. and 0.2 mg.

Solution Digitaline Nativelle, 1:1,000: 10 cc. glass stoppered bottles. Each 1 cc. contains 1 mg. of Digitaline Nativelle in a mixture of alcohol and glycerin.

THIAMINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1941, p. 551).

The following dosage forms have been accepted:

NATIONAL DRUG CO., PHILADELPHIA.

Tablets Thiamine Hydrochloride: 0.1 mg., 1 mg., 3.3 mg. and 6 mg.

Ampuls Solution Thiamine Hydrochloride, 3.3 mg. per cc.: 1 cc. and 10 cc.

Ampuls Solution Thiamine Hydrochloride, 10 mg. per cc.: 1 cc. and 10 cc.

Solution Thiamine Hydrochloride, 25 mg. per cc.: 5 cc. ampul-vials.

Solution Thiamine Hydrochloride, 50 mg. per cc.: 5 cc. ampul-vials.

Solution Thiamine Hydrochloride, 100 mg. per cc.: 5 cc. ampul-vials.

DIPHTHERIA TOXOID, ALUM PRECIPITATED (REFINED) (See New and Nonofficial Remedies, 1941, p. 464).

The following dosage forms have been accepted:

NATIONAL DRUG CO., PHILADELPHIA.

Refined Diphtheria Toxoid (Alum Precipitated): Marketed in packages of one 10 cc. ampul-vial representing five immunizations. For the two dose immunization treatment it is marketed in packages of one 2 cc. ampul-vial and two 10 cc. ampul-vials representing respectively one and ten immunizations. Contains merthiolate 1:10,000 as a preservative.

ASCORBIC ACID (See New and Nonofficial Remedies, 1941, p. 557).

The following dosage forms have been accepted:

PARKE, DAVIS & CO., DETROIT.

Tablets Ascorbic Acid: 100 mg.

Glaseptic Ampoules Solution of Ascorbic Acid: 2 cc. Each cubic centimeter contains 50 mg. of ascorbic acid and 0.1 per cent of sodium bisulfite added as a preservative.

SOLUBLE PENTOBARBITAL (See New and Nonofficial Remedies, 1941, p. 136).

The following dosage forms have been accepted:

FLINT, EATON & COMPANY, DECATUR, ILL.

Capsules Pentobarbital Sodium: 0.032 Gm. (½ grain), 0.0486 Gm. (¾ grain), 0.065 Gm. (1 grain), and 0.1 Gm. (1½ grains).

MENADIONE (See THE JOURNAL, Jan. 17, 1941, p. 226).

The following dosage form has been accepted:

S. M. A. CORPORATION, CHICAGO.

Tablets Menadione: 1 mg.

RIBOFLAVIN (See New and Nonofficial Remedies, 1941, p. 553).

The following additional dosage form has been accepted:

GEORGE A. BREON & CO., INC., KANSAS CITY, MO.

Tablets Riboflavin: 5 mg.

LIVER AND STOMACH PREPARATIONS (See New and Nonofficial Remedies, 1941, p. 328).

The following dosage form of Extract of Liver U. S. P. has been accepted:

ARMOUR LABORATORIES, CHICAGO.

Capsules Liver Extract Concentrate: 0.5 Gm. in 0.37 Gm. of corn oil. A suspension of extract of liver U. S. P. in corn oil marketed in capsules. Each capsule (0.5 Gm. of extract of liver) represents a potency of ⅛ U. S. P. oral unit.

NICOTINIC ACID AMIDE (See New and Nonofficial Remedies, 1941, p. 556).

The following product has been accepted:

MERCK & CO., INC., RAHWAY, N. J.

Nicotinamide (powder): ⅛ ounce, 1 ounce, ¼ pound and 1 pound bottles.

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SATURDAY, JULY 25, 1942

THE SUPPLY OF PHYSICIANS

As has been indicated previously in The Journal, many of the states have already given to the armed forces almost every physician that can be spared now. Some of the larger states must supply the personnel necessary for the immediate demands. Elsewhere in this issue (p. 1029) is notation of the establishment in several states of additional recruiting boards which are designed to aid the work of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians.

The letter circulated by the Procurement and Assignment Service has brought to the headquarters of that organization great numbers of return postal cards which indicate that many physicians have volunteered and are volunteering in response to the latest appeal. Nevertheless there is a distinct disparity between the applications coming through various routes directly to the Office of the Surgeon General of the Army, to the Air Force and to the Navy and the number that ought to be immediately available. Certainly the situation is not satisfactory when the armed forces are without a reserve pool from which to draw for an emergency. Everything possible is being done that can be done to hasten action on the applications of physicians through recruiting boards or directly through the Offices of the Surgeon Generals. The drive must continue, however, until some thousands of doctors have been commissioned who will be available for any contingency that may arise.

Again and again The Journal has pointed out that the needs of the armed forces will require that every physician under 45 years of age and physically fit who has not been stated by his state board of procurement and assignment to be engaged in an essential occupation must be made available to the armed forces. The Selective Service Act makes available to the armed forces every male citizen in the United States under 45 years of age. The physician who waits for the draft to pick him up certainly is in an unenviable light before his profession but even more in his own self respect. Little is to be gained by hesitating or holding back until the call comes, as it eventually will have to come from the boards of the Selective Service if the needs of the armed forces are not satisfied.

The Procurement and Assignment Service for Physicians, Dentists and Veterinarians was developed to aid the medical profession in determining for itself equitable distribution of medical service during the emergency. By utilizing its facilities, hospitals are being enabled to retain essential members of their staffs, industries are being enabled to retain necessary physicians and medical schools are being enabled to hold a sufficient number of their faculties to continue medical education. Everything possible is being done to enable individual communities to retain enough physicians to provide needed medical services for the civilian population. If, however, the armed forces do not get the medical personnel that they require the civilian population might be compelled to yield physicians who are doing their utmost to maintain civilian health. Let us realize that the winning of this war is the most important single objective ever placed before the medical profession of these United States and give to our nation the same complete wholehearted, voluntary service on which the nation has learned to depend in the past.

TOXICITY OF MERCURIAL DIURETICS

Recently a communication [1] was published in The Journal attributing the sudden death of 3 patients with congestive heart failure to the intravenous injection of a mercurial diuretic. The publication of this statement stimulated a review of the toxic manifestations and the fatalities that have been reported in connection with these widely used agents. In this issue of The Journal appear four reports.[2] The completeness with which consideration is given to various phases of the problem lends to this group of papers the aspect of a symposium. They should focus the attention of the medical profession on the need for care in the use of mercurial diuretics.

While the frequency of fatal accidents due to the mercurial itself is probably higher than has been supposed, the mortality attributable to the mercurial diuretics by any mechanism does not appear to be greater than, if indeed as great as, that reported for certain other potent drugs which are employed with equal frequency. The mechanism of sudden death in the small proportion of patients in whom the cause could be ascribed to the drug alone is explained by experimental studies on animals as

1. Friedfeld, Louis; Kissin, Milton; Modell, Walter, and Sussman, Ralph: Mercupurin, J. A. M. A. **117**: 1806 (Nov. 22) 1941.

2. DeGraff, A. C., and Nadler, J. E.: A Review of the Toxic Manifestations of Mercurial Diuretics in Man, this issue, p. 1006. Brown, George; Friedfeld, Louis; Kissin, Milton; Modell, Walter, and Sussman, R. M.: Deaths Immediately Following the Intravenous Administration of Mercupurin, p. 1004. Barker, M. H.; Lindberg, H. A., and Thomas, M. E.: Sudden Death and Mercurial Diuretics, p. 1001. DeGraff, A. C., and Lehman, R. A.: The Acute Toxicity of Mercurial Diuretics, p. 998.

either a primary poisoning effect of the mercury on the heart (ventricular fibrillation) or as respiratory failure secondary to the impaired cardiac action which is presumed to lead to anoxia through lowering of the blood pressure. However, in the majority of deaths reported following the use of mercurial diuretics the blame could be placed on the moribund condition of the patient, on digitalis poisoning due to mobilization of that drug in the blood stream from the edematous fluid removed by action of the mercurial, on the depletion of chloride resulting from previous diuresis, leading to oliguria or anuria and to faulty elimination of the diuretic itself, or on the presence of kidney impairment sufficient to prevent adequate excretion of the drug or to predispose to such damage by the mercurial. The largest proportion of the fatalities occurred among patients with evident kidney disease in which the use of mercurial diuretics is generally considered to be contraindicated. The comparatively rare idiosyncrasy to mercury compounds has been reported as a cause of death but apparently occurs with no greater frequency than with other drugs in susceptible patients. In the reports appearing elsewhere in this issue of THE JOURNAL it is suggested that the cutaneous eruptions produced by mercurial diuretics are now probably on an allergic basis rather than on the basis of a true mercurial dermatitis, since the latter is said to be no longer observed with the use of the more rapidly excreted theophylline containing mercurials on the market. Emphasis is placed on minor reactions, as well as the rare one suggestive of anaphylactic shock, as they may constitute a warning of more serious reactions if the mercurial agent is not discontinued.

The observations reported also indicate that change in the route of administration may not prevent the danger of accidents. The lack of deaths following the intramuscular or rectal administration of the mercurial may be due to the fact that the intravenous route is by far the one most commonly employed. Studies in animals of the comparative lethal doses of the commonly employed organic mercurial diuretics given at various intervals suggest that the sudden deaths reported in man probably cannot be avoided by slower injection or by dilution of the drug, nor can they be accounted for by the theophylline component or the concomitant administration of other drugs used in heart disease. The clinical observers further suggest that the striking wasting of the body of the edematous patient may account for the deaths on the basis of a relative overdose of mercury, although the animal experiments indicate that the size of the dose administered cannot be evaluated as a factor unless death occurs within the same time interval.

The deaths reported should serve to emphasize to the physician the importance of observing the known precautions in the use of these drugs. The investigators have made a praiseworthy attempt to bring these facts to the attention of the medical profession. As indicated in one of the reports, a possible method of treatment for the cardiac irregularities sometimes induced by the mercurial diuretics is under consideration. Further investigations may conceivably provide a means of eliminating even the danger of fatalities which cannot be avoided by the observance of known contraindications to the use of mercurial diuretics. The reported fatalities and toxic reactions should not discourage the rational use of mercurial diuretics. They should, however, serve as a warning and explanation of what to expect in rare instances or following promiscuous use of such agents.

THIAMINE IN THE AMERICAN DIET

In a recent contribution on the thiamine content of the American diet, Williams and his co-workers [1] state that their plan involved an attempt "to formulate a sequence of diets which contain all of the more important foodstuffs of the American dietary in proportions corresponding to the annual per capita consumption of each." Significance is given the conclusions through the use, as the principal basis of computation, of the extensive data of Stiebeling and Phipard [2] on diets of families of employed wage earners and clerical workers in cities. The assay was carried out by a modern chemical method supplemented, when indicated, by animal tests. With a daily intake of 2,500 calories as a basis for computation, the comparative contribution of the various food groups to the energy intake and to the total thiamine consumption is given.

The cereal products account for 47 per cent of the total daily calories and, when the white bread was not fortified with added vitamin, for 24 per cent of the thiamine. The dairy products, providing 18 per cent of the energy, give 21 per cent of the thiamine. Meat, which accounts for 15 per cent of the calories, is responsible for over 26 per cent of the thiamine, and of this total pork provides almost 22 per cent alone. The energy yielded by the vegetables is only 8.8 per cent, but the proportion of the total vitamin B_1 is high, namely 21.5 per cent. The fruits provide 4 per cent of the calories and 9 per cent of the thiamine. Corresponding to the total daily energy intake of 2,500 calories is a total vitamin B_1 intake of about 0.8 milligram.

The Food and Nutrition Board of the National Research Council has given 1.8 mg. of thiamine as the daily requirement of the adult. The data of Williams

1. Lane, R. L.; Johnson, Elizabeth, and Williams, R. R.: J. Nutrition **23**: 613 (June) 1942.
2. Stiebeling, H. K., and Phipard, E. F.: Circular 507, U. S. Dept. Agri., 1939.

and his co-workers indicate that the thiamine content of the average diet, such as was consumed by the middle two thirds or three fourths of the American people prior to the advent of enriched bread, would be considered inadequate at present. If enriched bread replaced the white bread in the diet under consideration, the vitamin B_1 would be raised to an intake of 1.3 milligrams a day, a value approaching a satisfactory level.

The foregoing discussion emphasizes the importance of bread, milk and meat as sources of thiamine in the average American diet. It adds support to various earlier contentions that our national diet is likely to be inadequate in this respect and demonstrates the possibility of bringing the intake of vitamin B_1 into the adequate range through the use of enriched flour.

Current Comment

USE OF SACCHARIN FOR SWEETENING

Sugar rationing and new emphasis on weight reduction have doubtless increased the use of saccharin for sweetening purposes. Renewed interest in the possible harmful effect of this substance is an apparent corollary. Earlier investigations of saccharin, however, have failed to reveal dangerous side-actions except from extremely large doses. Likewise the evidence does not reveal any reason why saccharin cannot be used continuously in average sweetening doses for an indefinite period. Many patients have taken saccharin for years without harmful effect.[1]

DEATH RATE CONTINUES TO DECLINE

Provisional mortality rates issued on July 3 by the Bureau of Census show that there was an actual decline in the number of deaths in the United States in 1941 as compared with the previous year, in spite of an increase in population. The total deaths in 1941 were 1,395,907, which is 21,362 less than the number reported for the registration area in 1940. Since 1933 all states have been included in the registration area, which lends a completeness to these figures that makes them more significant. Although it was generally true, with some important exceptions, that the states included latest were those with higher mortality, which tends to give an unfavorable bias to long time trends based on the registration area, this report shows that the death rate in the states included in this area has declined from 17.2 per thousand of population in 1900 to 10.5 in 1941. The highest death rate, 12.8, in 1941, was in cities of between 10,000 and 100,000 population. In cities of over 100,000 it was 11.7 and in rural districts 9.2. Death rates of less than 9 per thousand were found in Arkansas, North Dakota, South Dakota, Utah, Idaho, Oklahoma, Wyoming and North Carolina. The census report says of these rates "The differences in crude death rates between states do not necessarily indicate corresponding differences in health conditions. The age, sex and racial composition of the population differ between states, and these factors, among others, affect the crude death rate."

1. Wilcox, R. W.: The Therapeutics of Benzosulphinide, M. Rec. **98**: 595 (Oct. 9) 1920.

FIRST AID INSTRUCTORS ASSOCIATION

The members of a class for first aid instructors conducted by the U. S. Bureau of Mines at McPherson, Kan., in 1938 established an organization to promote first aid instruction in the petroleum industry. This organization has now grown into the Munsch National First Aid Instructors Association with chapters in Kansas, Oklahoma, Texas, New Mexico and Arkansas. Additional objects of the organization include the achievement of safety in the petroleum and allied industries, promotion of cooperation among employees and other organizations with similar objectives and dissemination of instruction on first aid and safety. The Bureau of Mines was not able to hold first aid classes among all or even a small percentage of employees in these widely scattered, small plants. The Munsch First Aid Instructors Association has trained six thousand, two hundred and forty employees for three hundred and forty-one companies, which far exceeds the number that the Bureau of Mines can reach under any other plan with the same number of instructors. The association has a national council, which is the governing body, state councils and district chapters. There are no dues. Each member aims to teach a first aid class each year. He organizes his own class regardless of company affiliations. Any person may become a member of the district chapter organization who has a U. S. Bureau of Mines first aid instructors card. The national association has adopted a constitution, insignia, lapel pins and merit bars, and awards in the form of bars have been planned by the national council. The esprit de corps among the members is high. The association has been valuable to its members, to the Bureau of Mines and to the many small oil companies. In some communities the chapters enter into civic and school activities, cooperate with the police in accident prevention programs, and make safety talks in schools and clubs. The members of one chapter built an emergency trailer equipped with first aid supplies and have conducted radio programs in their community in first aid and accident prevention. The instructors have carried out this training without remuneration, and those attending the classes do so at their own expense. Thus the work of the Munsch National First Aid Instructors Association must be limited. The association hopes, however, that the value of its work will be recognized and that donations of funds will be made to the national council. The U. S. Director of Civilian Defense has urged all communities to spread knowledge of first aid as widely as possible among the people. Last year the American Red Cross had more than thirty-five thousand first aid instructors throughout the country and during the year instructed a million persons in first aid.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

STATE HOSPITAL OFFICERS APPOINTED

The Medical Division of the Office of Civilian Defense announces the appointment of state hospital officers in coastal states to direct the hospital program of the Emergency Medical Service under the state chiefs of Emergency Medical Service. The following have received full time civil service appointments in the U. S. Public Health Service for these positions:

California: Mr. Thomas F. Clark, executive secretary, California Hospital Association, San Francisco.
Connecticut: Mr. William O. Sweeney, administrator, Windham Community Memorial Hospital, Willimantic.
Massachusetts: Mr. Oliver Pratt, administrator, Salem Hospital, Salem.
Pennsylvania: Major Roger A. Greene, administrator, Pottsville Hospital, Pottsville.
Virginia: Mr. M. Haskins Coleman, secretary, Richmond Hospital Service Association, Richmond.
Fourth Civilian Defense Region: Mr. John W. Rankin, Durham, North Carolina.

The following hospital officers have been appointed consultants in the Public Health Service for part time duty:

Maine: Mr. G. K. Lermond, Thomaston.
Maryland and District of Columbia: Mr. J. Douglas Colman, excutive director, Associated Hospital Service of Baltimore.
New Hampshire: Mr. Donald Steele Smith, administrator, Mary Hitchcock Memorial Hospital, Hanover.
New Jersey: Dr. Emil O. Frankel, division of statistics and research, State Department of Institutions and Agencies, Trenton.
Oregon: Mr. Ralf Couch, chairman, Hospital Service Council, Portland.
Rhode Island: Dr. George Matteson, Providence, general surgeon.
Vermont: Mr. Laurence Campbell, Barre, hospital trustee and a trustee of the New England Hospital Assembly.

The duties of these hospital officers will be to survey rural hospital facilities suitable for use as emergency base hospitals, to supervise personnel arrangements for the base hospitals and reception centers for evacuated civilians, to collaborate with state chiefs of the Emergency Medical Service in controlling movements of medical and nursing staffs as well as of casualties in any situation affecting emergency base hospitals and to perfect arrangements for transporting patients evacuated from casualty receiving hospitals.

RECRUITING BOARDS—SULFANILAMIDE—STUDIES OF WORLD AREAS

War Secretary Stimson told his press conference that every American soldier going into a theater of operations will be provided with a package of 5 Gm. of crystalline sulfanilamide to sprinkle on wounds in addition to twelve sulfanilamide tablets for internal use. He said the Army is increasing the number of medical department officers' recruiting boards to supply the need for additional doctors. Two additional boards have been authorized in New York, Pennsylvania and California, and one additional board in Massachusetts, Ohio and Illinois, while one board is functioning in each of the other states. A medical officer from the army air forces has been added to each of the twenty-nine recruiting boards to obtain doctors for the air service and a dental officer has been assigned to each board to assist in obtaining dentists. The recruiting boards may be located through local medical societies or the Surgeon General, Washington, D. C.

The Division of Medical Intelligence, Preventive Medicine Service, Office of the Surgeon General, has prepared a series of studies covering four general world areas on health, sanitation and climatic conditions. These instructions are being issued to military attachés and members of military missions, as well as to medical officers of overseas forces, to protect the health of U. S. soldiers sent to those regions. Subjects treated include water consumption safety precautions, protection against mosquitoes and other insects that carry disease, prevention of diseases indigenous to the various regions, bathing precautions, care of the skin and feet, selection of suitable clothing, prevention of sunstroke, energy conservation and health maintenance under desert or tropical conditions, prevention of illness from food spoilage or contamination and many other hygienic precautions.

Secretary Stimson said that the Women's Army Auxiliary Corps now has two contract nurses and, as the corps increases, female medical officers may be inducted into the corps or will be contracted at the rate of five for every thousand women.

WIDESPREAD RESPONSE OF PHYSICIANS IN NEW YORK

A survey by the New York State Medical Society, made public July 5, covering 98 per cent of the population of the state, gave assurance that the medical needs of every community will be protected. The survey disclosed the number of doctors already in active military service and the number of others who have been commissioned and are awaiting orders. The process of obtaining this personnel and at the same time of protecting the local communities offers assurance that the needs of the government will be met. The survey was made by direction of the Council of the New York State Medical Society and was conducted by the Medical Preparedness Committee. The chairman, Dr. Louis H. Bauer, pointed out that the setup under which they are working is for local medical societies to determine who is and who is not essential. Physicians are not taken into the service until released by the community in which they live. The survey showed that a total of 6,000 have already been released by these county committees in addition to those now in active service.

EMPLOYMENT OF HANDICAPPED WORKERS

Since the establishment of the War Manpower Commission in April, conferences have been held by the U. S. Office of Education, the U. S. Employment Service and the Division of Industrial Hygiene to consider the employment of physically handicapped persons in the war industries. Recommendations have been made to the War Manpower Commission, and a letter to employers calling for review and revision where necessary, of existing physical standards for employment, awaits the signature of the commissioner. The policy enunciated in this letter would require the employment of many thousands of persons with minor or major disabilities and would make the preemployment physical examination an effective tool for the proper placement of all workers.

FILM STORY ABOUT NAVY PHYSICIAN

According to news reports from Hollywood (Brady, Thomas F.: New York *Times*, June 28) the life and recent experiences of Dr. Corydon M. Wassell, naval medical corps, will be used as the basis for a new moving picture. Dr. Wassell, it will be recalled, was individually named for his heroic work in the battle of Java in a radio broadcast by President Roosevelt. The movie, it is said, will emphasize Dr. Wassell's work between February 4, the date of the action by the *Marblehead* and the *Houston*, and March 13, when he and eight wounded men arrived in Australia on board the last small ship out of Java. It has been announced that the Navy Relief Society has already received a $50,000 advance against an undisclosed percentage of the gross rentals of the picture.

MORE NURSES' AIDES NEEDED

As of June 20, 25,905 nurses' aides have been enrolled toward the goal of 100,000. The Office of Civilian Defense has asked its regional office representatives to work out plans for stimulating the recruitment of nurses' aides to meet war demands. A recent memorandum reveals that some hospitals are reported to be accepting volunteer workers without training and permitting them to carry out many of the tasks usually performed by nurses' aides. Such a practice, it was said, militates against the establishment of a reliable disciplined corps of workers and deters enrolment of nurses' aides.

Nurses' aides are recruited by the American Red Cross in cooperation with the local civilian defense volunteer offices. The training course includes eighty hours of instruction presented in seven weeks, the first half being given in the Red Cross headquarters and the other half in hospitals selected as training centers. Nurses' aides agree to give one hundred fifty hours of service in each calendar year; but, in case of need for war service, they must be prepared to serve locally in emergency for as long as needed. The goal of 100,000 trained nurses' aides must be reached. The medical division of the Office of Civilian Defense declared that in no other branch of service can women be of greater value to the war effort.

STATE CIVILIAN DEFENSE MEDICAL OFFICIALS COMMISSIONED IN PUBLIC HEALTH SERVICE

To facilitate the emergency program being developed by the Medical Division of the Office of Civilian Defense and the U. S. Public Health Service, physicians who are state and deputy state chiefs of Emergency Medical Service in most of the coastal states have been commissioned in the Public Health Service Reserve so that they may exercise both state and federal responsibilities. Where a state chief of Emergency Medical Service is unable to give full time to this activity, his commission is to remain on an inactive status and he is provided with a deputy commissioned in the active reserve who is called immediately to full time service. These officers will have as their first duty the stimulation and guidance of local chiefs of Emergency Medical Service in the organization of casualty receiving hospitals and field casualty services. They will serve also as responsible agents of the states and of the medical division of the Office of Civilian Defense and of the Public Health Service for the organization of emergency base hospitals. These officials will determine, in collaboration with the local military and the state evacuation authorities, the lines of evacuation and means of transport of civilian casualties and other hospitalized persons from local casualty receiving hospitals to emergency base hospitals. These officers also will review and certify bills to be submitted to the Public Health Service for payment for the hospital care of civilian casualties.

As of July 1, the following have been commissioned in the active reserve of the Public Health Service as state or deputy state chiefs of Emergency Medical Service to carry out this program:

Alabama: Dr. John Newdorp, Montgomery, deputy state chief.
California: Dr. Charles F. Sebastian, Los Angeles, state chief.
Connecticut: Dr. Ralph E. McDonnell, New Haven, deputy state chief.
Florida: Dr. Gilbert S. Osincup, Orlando, state chief.
Georgia: Dr. Edwin R. Watson, Atlanta, deputy state chief.
Maryland: Dr. Arthur J. Lomas, Baltimore, deputy state chief.
Massachusetts: Dr. Andre W. Reggio, Chestnut Hill, deputy state chief.
New Jersey: Dr. Gerald W. Sinnott, Jersey City, deputy state chief.
North Carolina: Dr. Sylvester D. Craig, Winston-Salem, deputy state chief.
Oregon: Dr. Vernon A. Douglas, Salem, state chief.
South Carolina: Dr. H. Grady Callison, Columbia, deputy state chief.
Washington: Dr. Arthur E. Lewis, Seattle, deputy state chief.

In New York Dr. Randolph A. Wyman, Brooklyn, has been commissioned to serve as deputy city chief.

In certain cases state chiefs on part time duty have been appointed consultants in the Public Health Service. Thus far these include:

New Hampshire: Dr. Charles H. Parsons, Concord.
Delware: Dr. Meredith I. Samuel, Wilmington.
Virginia: Dr. Edgar C. Harper, Richmond.

Mr. Lee Mailler, New York, chairman of the State Health Preparedness Commission, under which the Emergency Medical Service of New York State has been developed, has been appointed a special consultant.

MEDICAL RECRUITING BOARD

In conjunction with the Office of Procurement and Assignment for the District of Columbia, a Medical Recruiting Board has been established at the headquarters of the District of Columbia Medical Society, 1718 M Street N.W., Washington, D. C. The board consists of Lieut. Col. Willard C. Goley, M. C., U. S. Army, and Major William H. Phillips of the infantry, representing the adjutant general. Dr. Francis X. McGovern is procurement and assignment officer for the District. Letters have been sent to four hundred physicians up to the age of 45 in the District who have been considered available for military service, requesting them to come to the medical society building for interviews concerning commissions in the Medical Corps of the Army. This method of recruiting of physicians has been resorted to in view of the immediate need of the armed forces for more medical officers.

CONSULTANTS ON BLOOD AND PLASMA PROGRAM

Under the program launched by the Medical Division of the Office of Civilian Defense and the U. S. Public Health Service to provide plasma for the treatment of civilians injured in warfare, regional consultants have been appointed to advise hospitals on technical problems related to the establishment of blood and plasma banks.

Dr. Fred Bryan, Rochester, N. Y., is the consultant for the first and second civilian defense regions and a part of the third region. Dr. John Elliott, Salisbury, N. C., will serve in the fourth and eighth regions and the remainder of the third. Dr. Emeric Dobos, Senior Surgeon (R), U. S. Public Health Service, is on active duty in the ninth region. Dr. Elmer L. DeGowin, Iowa City, is acting as technical consultant on special problems. The blood and plasma bank program is at present confined to vulnerable areas within 300 miles of the ocean and gulf coasts. The Subcommittee on Blood Substitutes, Division of Medical Sciences, National Research Council, serves in an advisory capacity to the Medical Division of the Office of Civilian Defense, as it does to the medical departments of the Army and Navy and the American Red Cross.

NEW YORK HOSPITAL UNIT

The trustees of Cornell University and the governors of the Society of the New York Hospital gave a dinner, July 14, at the Hotel Roosevelt in New York City to the physicians and nurses who were inducted the following day as the staff of a general hospital of the U. S. Army. These physicians and nurses were from the staffs of the New York Hospital and Cornell University Medical College. The military hospital will bear the same number as the New York Hospital unit in the first world war. About two hundred persons attended the dinner. Among the speakers were Lieut. Col. Ralph F. Bowers, director of the hospital unit, who was a member of the surgical staff of New York Hospital; Langdon P. Marvin, acting president of the Society of the New York Hospital, and Roger Williams, a trustee of Cornell University, who said that New York Hospital has a long record of service to the wounded, its first patients having been soldiers of General Washington's army admitted on July 12, 1776 after the bombardment of the battery in New York City. New York Hospital also cared for seamen wounded in the War of 1812, for soldiers in the Civil War and it sent a unit to Puerto Rico in the Spanish-American War.

CHEMICAL WARFARE TRAINING CENTER

The War Department has announced, according to the *Army and Navy Journal*, that a chemical warfare training center is to be established in the South on a 30,000 acre site. The initial accommodations will be for five thousand men, which may be increased if necessary. After completion of the courses given at the training center the men will be assigned to duty with chemical warfare units throughout the Army.

"GUIDES TO THERAPY FOR MEDICAL OFFICERS"

A technical manual for medical officers has just been issued by the Government Printing Office in Washington, entitled "Guides to Therapy for Medical Officers." The material on which the text of the manual is based was furnished largely by the various committees and subcommittees of the Division of Medical Sciences of the National Research Council with the assistance of other consultants. A preliminary note gives the names of all the various specialists who cooperated in producing this book. The final editing was done by Dr. R. N. Nye of the Committee on Information of the Division of Medical Sciences of the National Research Council. The book is divided into seven sections, covering a general consideration, surgical emergencies, medical emergencies, diagnosis and treatment of venereal diseases, chemotherapy and serotherapy in certain infectious diseases, treatment and control of certain tropical diseases, and the rickettsial diseases. Here in outline form is a compilation of the very latest information available on the subjects discussed as standardized for use under Army conditions. The book constitutes, therefore, an invaluable reference work for the Army medical officer and will be found most valuable by any physician under any circumstances. Copies of the book are available from the Superintendent of Documents, Washington, D. C. The price is 25 cents.

MASONS PRESENT AMBULANCES TO RED CROSS

At a ceremony held, on account of inclement weather, in the New York City council chamber on June 27 the Masonic order of New York State presented eleven ambulances and a check for $25,343 to the American Red Cross, which was accepted by its chairman, Hon. Norman H. Davis. The mobile units were inspected by Mr. Davis, Mayor La Guardia and Masonic officers. In his speech, Mr. Davis disclosed that negotiations were then pending for the operation of a "mercy ship" in the Pacific Ocean to carry, under the supervision of the International Red Cross Committee, food, clothing and other needed articles to United States prisoners of war and civilians interned in Japan and elsewhere in the Far East. Mr. Davis said that some parcels had already been dispatched to the prisoners of war in Japan.

GRADUATES IN AVIATION MEDICINE UNDER NEW SYSTEM OF TRAINING

The course of instruction in aviation medicine for aviation medical examiners is now divided into two parts, the didactic portion being conducted at one field and the practical portion at three army air forces classification centers. The first class to graduate under this new system of training was graduated on July 2. Appropriate exercises were held in each of the centers. The list of graduates follows:

ALABAMA

John H. Lary, Captain, Huntsville.
Reuben J. Maxwell, 1st Lieut., Sulligent.

ARKANSAS

Byron Z. Binns, 1st Lieut., Monticello.
Coy C. Kaylor, 1st Lieut., Van Buren.

CALIFORNIA

Donald C. Collins, Major, Beverly Hills.
Halle O. Hall, 1st Lieut., Beverly Hills.
William F. Harding, Captain, Sacramento.
John T. Klausner, Captain, Los Angeles.
Francis B. O. Morris, 1st Lieut., Santa Barbara.
Albert D. Phillips, Major, Sacramento.

COLORADO

George A. Peabody, 1st Lieut., Denver.
Perry G. Pratt, Captain, Denver.
Charles E. Walker, Major, Denver.

CONNECTICUT

Harold I. Harvey, 1st Lieut., New Britain.
Gerald Krosnick, 1st Lieut., New Haven.

DELAWARE

Joseph S. McDaniel, 1st Lieut., Dover.

DISTRICT OF COLUMBIA

Nicholas F. Atria, Captain, Washington.
L. Render Braswell, Major, Washington.
Robert S. Brua, Major, Washington.
John M. Collins, Captain, Washington.
Richard I. Crone, Captain, Washington.
Donald H. Earl, Captain, Washington.
Everett C. Freer, Captain, Washington.
Wendell P. Harris, Captain, Washington.
Aubrey L. Jennings, Major, Washington.
Russell S. Leone, Major, Washington.
John J. Meany, Captain, Washington.
Franklin L. Spann, Captain, Washington.

GEORGIA

James W. Merritt Jr., 1st Lieut., Gainesville.
Fred E. Murphy, 1st Lieut., Jessup.
Glenn W. Pennington, 1st Lieut., Mathews.

ILLINOIS

Donald W. Anderson, 1st Lieut., Chicago.
Leon J. Armalavage, 1st Lieut., Chicago.
Robert E. Bowen, 1st Lieut., Chicago.
Milton J. Loring, 1st Lieut., Chicago.
Robert J. Stephen, 1st Lieut., Joliet.
Anthony J. Sweeney, 1st Lieut., Chicago.

INDIANA

Paul A. Clouse, 1st Lieut., Evansville.
John M. Palm, Captain, Brazil.

IOWA

Vance J. Elliott, Captain, Knoxville.
Elmer M. Smith, Captain, Granger.

LOUISIANA

Chester S. Fresh, Major, New Orleans.

MASSACHUSETTS

Arthur J. Hadler, 1st Lieut., Boston.
Jonathan I. Morrison, 1st Lieut., Newton.

MICHIGAN

Cecil D. Conrad, 1st Lieut., Ypsilanti.
James E. Forsyth, 1st Lieut., Albion.
Roelof Lanting, 1st Lieut., Gladwin.
Alexander Vida, Captain, Detroit.

MINNESOTA

Kenneth E. Bray, Captain, Biwabik.
William P. Gjerde, 1st Lieut., Staples.

MISSOURI

Anthony V. Benincasa, 1st Lieut., St. Louis.
Williston P. Bunting, 1st Lieut., Kansas City.
Earl E. Miller, Captain, Kansas City.

MONTANA

Thaddeus F. Bush, 1st Lieut., Butte.
Raymond O. Lewis, 1st Lieut., Roundup.

NEBRASKA

John H. Easley, Captain, Lincoln.
Richard H. Schaefers, Captain, Omaha.

NEW JERSEY

Sam Lemkin, 1st Lieut., Newark.
William D. O'Gorman, Captain, Jersey City.

NEW YORK

Louis L. Amato, Captain, New York.
Charles A. R. Connor, 1st Lieut., New York.
Alfred H. Dobrak, 1st Lieut., Buffalo.
Fredric Lewis, Captain, New York.
Edmund F. Longworth, 1st Lieut., Pelham.
Hubert S. Senne, 1st Lieut., Glendale.
Charles S. Yavelow, 1st Lieut., Mount Vernon.

OHIO

Edwin E. Ash, 1st Lieut., Forest.
Attilio D. Puppel, 1st Lieut., Ashley.
Herman M. Turk, Captain, Euclid.

OREGON

Max W. Hemingway, Captain, Bend.
Herbert D. Lewis, Captain, Hood River.
Richard W. Lyman, 1st Lieut., La Grande.
Charles P. McKim, 1st Lieut., Baker.
Weldon T. Ross, 1st Lieut., McMinnville.

PENNSYLVANIA

Frank L. Bracken, 1st Lieut., Westmont.
Robert M. Laughlin, 1st Lieut., Pittsburgh.
Joseph W. Mendoza, Captain, Harrisburg.
Paul H. Rankin, Captain, Sharpsville.
Howard M. Scull, 1st Lieut., Langehorne.
George C. Wassell, Captain, Pittsburgh.

SOUTH CAROLINA

James E. Lipscomb, Captain, Greenville.

SOUTH DAKOTA

Lindsay J. Ervin, 1st Lieut., Montrose.
Ryland M. Jacobus, 1st Lieut., Letcher.

TENNESSEE

Willard D. Bennett, 1st Lieut., Nashville.
Melvin M. Simmons, 1st Lieut., Nashville.
Jehu C. Walker, Captain, Savannah.

TEXAS

Sam H. Dryden, Captain, Abilene.
Earl K. Gill, Major, Corpus Christi.
Carl F. Goeth, Captain, San Antonio.
Samuel H. Haigler, 1st Lieut., Austin.
Haskell D. Hatfield, Major, El Paso.
Benjamin B. Hutchinson, 1st Lieut., Lubbock.
Ulen G. Medford, 1st Lieut., Lufkin.
William C. Smith, 1st Lieut., Lockhart.
Afton N. Wilkins, Captain, Conroe.

UTAH

Clarence C. Hetzel, Captain, Ogden.
Rulon F. Howe, 1st Lieut., Murray.
Vernal H. Johnson, Captain, Ogden.

VIRGINIA

Charles P. Alexander, Captain, Richmond.

WASHINGTON

Louis D. Fey, Captain, Seattle.

WISCONSIN

Edward H. Loveroos, Captain, Superior.
Mancel T. Mitchell, Captain, Eau Claire.
Oscar C. Olson, Captain, Madison.
Julius A. Roth, Captain, LaCrosse.

WYOMING

Paul F. Miner, 1st Lieut., Laramie.

CUBA

Roberto Covas y Coro, 1st Lieut., Havana.
Risley F. Haines, 1st Lieut., Boyamo.

ORGANIZATION SECTION

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 7378, the Revenue Act of 1942, has been passed by the House of Representatives. The normal tax rate on individuals, it is proposed, will be 6 per cent instead of 4 per cent as under existing law. The surtax will start at 13 per cent instead of 6 per cent for the first $2,000 surtax net income, with a constant increase in the rate for incomes in the higher brackets. The personal exemption for a single person will be $500, for a married person $1,200. Deductions for dependents will remain as in the existing law at $400. A new provision authorizes an additional deduction for persons in the military or naval service by exempting from taxation so much of the amount received during the present war by an individual in the military or naval forces as salary or compensation in any form from the United States for active service in such forces as does not exceed $250 in the case of a single person and $300 in the case of a married person. The bill proposes no change in the earned income credit. No authorization is made for the deduction of expenses incurred for medical care as had been recommended by the Treasury Department, nor does the bill provide for the taxation of certain income of charitable and other exempt corporations, as had also been suggested by the Treasury Department. The bill does provide for relief in the manner of the treatment of income accruing on the death of a taxpayer. Heretofore, accounts receivable on the books of the taxpayer at the time of his death have been accrued for income tax purposes for the year in which death occurred, resulting in inequitable burdens on the estates of the deceased taxpayers who had reported their incomes on a cash receipts and disbursements basis. The pending bill proposes that such accounts will be taxable as collected, the tax to be paid by the persons who actually receive the money. H. R. 7239 has passed the House, authorizing the Director of the Census to issue certifications of birth records.

Bills Introduced.—S. 2654, introduced by Senator Pepper, Florida, proposes to authorize the Federal Security Administrator to establish and maintain a system for recording the dates and places of birth of individuals within the United States. H. R. 7379, introduced by Representative Allen, Louisiana, proposes that the United States shall, in addition to hospitalization and medical care now authorized by law, provide vocational training for all disabled veterans at public expense. H. R. 7396, introduced by Representative Gearhart, California, provides for vocational rehabilitation and return to civil employment of disabled persons discharged from the military and naval forces. H. R. 7398, introduced by Representative Costello, California, proposes to authorize an appropriation not to exceed the sum of $2,600,000 to construct a fireproof marine hospital for the accommodation of approximately 300 bed patients in or near Los Angeles.

WOMAN'S AUXILIARY

Colorado

The Woman's Auxiliary to the Boulder County Medical Society, which was organized in 1940, now has a paid membership of thirty. The members are from Boulder, Longmont, Louisville and Frederick. Four *Hygeia* subscriptions have been placed in Boulder County rural schools. All members of the auxiliary are busy with some form of Red Cross work.

Illinois

The Adams County auxiliary has been placed in charge of the Blood Donor Service in the county by the American Red Cross. The women of the auxiliary also assist a mobile unit which is sent to Quincy from St. Louis.

Iowa

Sixty-eight members attended a meeting of the Woman's Auxiliary to the Polk County Medical Society, March 3, at which Dr. Thomas A. Burcham of Des Moines spoke on "The Work of the Iowa Industrial and Defense Commission." A contribution to the Nurses Student Loan Fund was voted. The auxiliary decided also to provide hostesses twice a month for the U. S. O. Recreation Center in Des Moines and to serve refreshments.

The auxiliary to the Waterloo Medical Society met at the home of Dr. and Mrs. John E. O'Keefe in Waterloo. Twenty-six members were present. Mrs. William R. Hornaday of Des Moines, state president, spoke on the Nurses Student Loan Fund.

New York

The Oswego County auxiliary gave a $50 donation to the Red Cross, the proceeds from the fashion show.

At a recent meeting of the Queens County auxiliary a $10 donation was given to the Red Cross War Fund Drive.

West Virginia

Mrs. B. D. Smith presided and twelve members attended a recent meeting of the Logan County auxiliary. Dr. E. W. Smith, secretary for Foreign Mission, addressed the group on "Mexico."

Mrs. Traul, chairman, reported on the recent benefit bridge party. A total of $97.74 was raised for the Red Cross fund.

The Woman's Auxiliary to the Marion County Medical Society held an all day health institute recently in Fairmont. During the morning Mrs. Howard Jones and Mary Jane Minnis, R.N., spoke on "Prenatal Clinics"; H. S. Burnette, D.D.S., on "Dental Hygiene"; Mrs. W. A. Welton, Marguerite Hays, R.N., and Ethel Elfenbein, R.N., on "Well Baby Conference"; Dr. C. F. McClintic on the "State Department of Health"; Dr. A. M. Price on "Communicable Diseases"; Dr. J. W. Davis on "Marion County Health Program," and Mr. W. B. Kirchman on the "City Water Department."

After luncheon, Dr. K. Y. Swisher, president of the Marion County Medical Society; Miss Mabel W. Perry of the State Bureau of Nutrition, and Dorothea Campbell, director of the Bureau of Health Education, spoke on "Pooling Our Resources for Health Education"; Dr. Justus Pickett on posture; Florence Kneisel and May Gribble, R.N., on "Red Cross Nursing," and Mr. Floyd Prunty on "Marion County Board of Education." "White Battalion," a movie, was shown by the Fairmont General Hospital and a first aid demonstration was given by the Koppers Coal Company first aid team.

Dr. Swisher presided at dinner, after which Dr. Louis B. Leplace, chief, Department of Pediatrics, Jefferson Medical College of Philadelphia, spoke on "The Art of Growing Old."

The auxiliary placed health exhibits in the public rooms of the hotel. More than five hundred persons attended the lectures and the exhibits.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Grant for Research in Ophthalmology.—The Columbia Foundation, San Francisco, has given $20,000 to finance a research project in ophthalmology at the Mount Zion Hospital Research Laboratories, San Francisco, under the direction of Drs. Frank H. Rodin and Charles Weiss. The work will include a study of bacteriology and immunology of the eye. First it is planned to study the flora of the normal eye and of the common eye diseases. Later the study of special problems will be undertaken. The Columbia Foundation was established in 1940 in the interest of educational, cultural and philanthropic activities, internationally.

COLORADO

State Society Cancels Annual Meeting at Colorado Springs—A telegram signed by Drs. Guy C. Cary and Ralph S. Johnston, president and president-elect, respectively, of the Colorado State Medical Society announces that the board of trustees has voted unanimously to cancel the annual session of the society which was scheduled to be held in Colorado Springs, September 23-26. This action was taken in view of the governmental request for curtailment of all travel not vital to the war effort and in view of the fact that many of the physicians who would have attended the annual session will be in the military service while those not in military service must remain close to their civilian duties. The house of delegates of the Colorado State Medical Society, however, will meet in Denver, September 23, to transact the necessary annual business and coordinate medical military activities in Colorado.

CONNECTICUT

Personal.—Ira V. Hiscock, C.P.H., was elected president of the New Haven Board of Health at a meeting on June 17 to succeed the late Mrs. Edward G. Buckland. Mrs. Samuel C. Harvey and Dr. William C. McGuire have been named members of the board to succeed Mrs. Buckland and the late Dr. James D. Trask.

State Medical Election.—Dr. George M. Smith, Pine Orchard, was named president-elect of the Connecticut State Medical Society, May 20, and Dr. Roy L. Leak, Middletown, was inducted into the presidency. Dr. Creighton Barker, New Haven, was reelected executive secretary. New Haven was selected as the place of the next annual session in May 1943.

Physicians Honored.—Physicians from Norwalk, Stamford, Danbury and Bridgeport gave a dinner in Westport recently to honor Dr. William S. Stone, who was presented with a gold plaque on behalf of the Norwalk Medical Society. The inscription on the plaque stated that the testimonial was "in deep appreciation of his humanitarian and scientific efforts on behalf of this community."——The new Louis I. Mason Memorial Nurses' Home at the Windham Community Memorial Hospital, Willimantic, was opened with appropriate ceremonies recently. The home was given by the widow of Dr. Mason as a memorial to him. Dr. Mason died in 1930, aged 64.

ILLINOIS

Society News.—At its recent annual meeting in Chicago on May 9 the Illinois Psychiatric Society elected Drs. Francis J. Gerty president, Franz G. Alexander vice president and Eugene I. Falstein secretary-treasurer. All are of Chicago.

Chicago

Course in Electrocardiography.—Michael Reese Hospital will offer a full time course in electrocardiography, August 17-29, under the direction of Dr. Louis N. Katz, director of cardiovascular research. Additional information may be obtained from the hospital. There will be sessions on interpretations of electrocardiograms, and emphasis will be placed on chest leads and on the importance of the electrocardiogram in coronary sclerosis and myocardial infarction.

Dr. Fred Adair to Retire as Professor.—Dr. Fred L. Adair, chairman of the department and Mary Campau Ryerson professor of obstetrics and gynecology, University of Chicago School of Medicine, and chief of service at the Chicago Lying-In Hospital, will retire on October 1, having reached the age of retirement. He will be succeeded by Dr. William J. Dieckmann, associate professor in the department. Dr. Adair, who was born in Iowa in 1877, graduated at Rush Medical College in 1901. He became associated with the University of Minnesota in 1905, serving there as professor of obstetrics and gynecology from 1926 to 1929. He was secretary of the Section on Obstetrics and Gynecology of the American Medical Association from 1928 to 1931 and chairman from 1931 to 1932. In 1922 Dr. Dieckmann graduated at Washington University School of Medicine, St. Louis. He later served in various capacities in the department of obstetrics, resigning in 1929 to join the Chicago faculty.

KANSAS

New Psychiatric Group.—The Kansas Psychiatric Society was organized at an informal meeting, April 9, at the Hotel Kansan, Topeka. At the first regular meeting, April 22, Dr. Robert P. Knight, Topeka, was elected president and Dr. Edward D. Greenwood, Topeka, secretary-treasurer. The new society will have about thirty charter members and will hold quarterly meetings.

Changes in Health Personnel.—Dr. David D. Carr, formerly a member of the Utah State Board of Health, Salt Lake City, has been named full time health officer of Topeka, effective June 1.——Dr. Carl W. Plowman, Jewell, has been appointed health officer for Jewell County, succeeding the late Dr. Spencer B. Dykes, Esbon.——Dr. Denman T. Gammell, Ulysses, has been named health officer of Grant County.

MICHIGAN

Beaumont Room in Detroit.—The Wayne County Medical Society, Detroit, has set aside a room in its headquarters to be developed as the Beaumont Room. The lectureship foundation committee, which for a number of years has been arranging the annual Beaumont lectures for the society, is collecting material to be displayed permanently in the room and it is planned to hang there a painting of Beaumont which is now being made by Dean Keller. The painting is to be a replica of the one which hangs in the Cushing Library at Yale University School of Medicine, New Haven, Conn. It is hoped that when the next Beaumont lectures are delivered, probably early in 1943, the portrait will be hung and Beaumont memorabilia will be ready for exhibition. The committee has already received a first edition of Beaumont's book, two editions of Paré's "Opera" and some other valuable items from an anonymous donor. The committee has been authorized by the society to accept any gifts which interested persons may wish to donate to the collection.

NEW JERSEY

Radiologists Choose Officers.—The Radiological Society of New Jersey chose the following officers at its recent annual meeting: Dr. William J. Marquis, Newark, president; Dr. Herbert A. Vogel, Elizabeth, vice president; Dr. Harry J. Perlberg, Jersey City, secretary, and Dr. Charles P. Oderr, Westfield, treasurer.

NEW YORK

Society Limits Rounds of House Calls.—The Cayuga County Medical Society has announced a policy, aimed at conserving fuel and rubber, which limits the calls of its members to two regular rounds of house calls, one in the morning and one in the afternoon. Emergency calls will be taken care of at any hour, but routine visits will be reduced to these two calls, according to newspaper reports May 19.

Physician Honored.—Dr. Irving W. Potter, Buffalo, was honored on July 7 when a bronze plaque was unveiled in the new obstetric wing of the Millard Fillmore Hospital, Buffalo. The speakers at the ceremony included Drs. James E. King, professor emeritus of gynecology at the University of Buffalo School of Medicine; Charles J. Reynolds, who for thirty-five years has served as anesthetist to Dr. Potter, and George A. Himmelsbach, Buffalo. Dr. Potter is a past president of the Medical Society of the County of Erie and the Buffalo Academy of Medicine and formerly served as chief of the obstetric department of the hospital.

New York City

Personal.—Dean Sage Jr., attorney, has been appointed executive vice president of the United Hospital Fund of New York.——Dr. Luthero Vargas of Brazil was guest of honor at a dinner given on June 29 at the New York Academy of Medicine under the auspices of the members of the Inter-American Division of the Academy and of America Clinica. Dr. Vargas has been visiting various hospitals throughout the United States in recent months to assemble ideas to include in

his new wing of orthopedics for the treatment of school children at the Centro Medico Pedagogico Oswaldo Cruz of Rio de Janeiro.——Dr. Robert L. Dickinson, formerly president of the American Gynecological Society, has recently been appointed a life fellow of the association.

A Million for Public Health Research.—The Public Health Research Institute of the City of New York, Inc., will receive $100,000 a year for ten years for its researches on public health, according to authorization of the board of estimate announced in the New York *Times*. The city and the institute, a nonprofit scientific institution, have entered into a contract which went into effect July 1 and is automatically renewable for similar periods of ten years unless previously abrogated. The money is to be used by the institute to carry on fundamental medical research by a staff of competent scientists under the direction of a research council composed of authorities in the fields of medicine, biology, physiology, nutrition, public health and related fields. The contract was signed after the legislature passed a bill authorizing cities to enter such contracts with nonprofit scientific institutions to carry on "research into matters pertaining to public health." Under the contract, the services to be rendered by the institute include the following:

Research and investigation into the control of diseases such as influenza, poliomyelitis, arthritis, degenerative diseases and general physiologic problems such as nutrition.

Generally to engage in laboratory experimentation and research in order to develop better and more economical biological products and improved technical procedures for use in combating diseases and epidemics.

To aid and assist the director of the bureau of laboratories of the department of health in matters involving public health research.

The city, on its part, agrees "to permit the institute to use and to make available for such use part of the premises now occupied by the bureau of laboratories of the department of health at the William Hallock Park Laboratory, or any other building or premises owned, leased or controlled by the city suitable or proper for laboratory investigation and research, during the term of this agreement or its renewal, without any charge for rent, water, heat, light, janitorial services and maintenance. The annual payments of $100,000 for the ten year period will be paid in quarter annual payments each year. The results of the institute's research "shall be the property of the city." Any discoveries of products or methods shall belong to the city as soon as made, for which there shall be no compensation. All patents issued to the city or to any of its employees shall be assigned immediately to the city, for which there shall be no compensation. David M. Heyman is president of the board of directors of the institute. Other members include the mayor, the controller, Health Commissioner John L. Rice, David Rockefeller, vice president, Edwin F. Chinlund, treasurer, and David Morse, secretary. The research council, in charge of all scientific programs, will be directed by Dr. Thomas M. Rivers of the Rockefeller Hospital. Other members are Dr. Eugene L. Opie, Dr. Henry L. Sherman, Dr. George Baehr, Michael Heidelberger, Ph.D., and Dr. Ralph S. Muckenfuss, director of the bureau of laboratories.

OHIO

Fifty Years of Practice.—The Tuscarawas County Medical Society gave a dinner in New Philadelphia, June 11, in honor of Drs. Clarence D. Kurtz, New Philadelphia, and George B. Kistler, Newcomerstown, who have completed fifty-one and fifty years, respectively, in the practice of medicine. Other members of the society who have completed fifty years in the practice of medicine and who bring the total to seven are Drs. Elliott D. Moore, New Philadelphia, fifty-five years; James M. McCollam, Uhrichsville, fifty-three years; Joseph Blickensderfer, New Philadelphia, fifty-two years; Byron G. Anderson, Uhrichsville, fifty-five years, and George A. Henry, Tuscarawas, fifty-one years.——Dr. Mark Millikin, Hamilton, was guest of honor at a dinner, May 27, given by the Butler County Medical Society to observe his completion of fifty years in the practice of medicine. He was presented with a gold watch by the society. The speakers included Dr. Wilmer E. Griffith, Hamilton, secretary emeritus of the society, and Dr. Martin H. Fischer, Cincinnati.

Physicians Seek to Incorporate Medical Care Plan.—Nine physician members of the Academy of Medicine of Cleveland have submitted to the secretary of state papers for incorporation of a medical care plan to be known as the Cleveland Medical Service Association, according to the Cleveland *Plain Dealer*, June 20. The physicians are Drs. Harry V. Paryzek, former president of the state medical association; John E. Rauschkolb, president of the academy; Richard Dexter and Jacob E. Tuckerman, former presidents; Edward F. Kieger and William E. Hill, directors of the academy; Demba M. Spicer, Lakewood, a member of the academy's committee on economics; Milton B. Cohen, and Dwight S. Spreng, chairman of the economics committee. The newspaper pointed out that, since a recent vote by the academy on a medical care plan lost by only five votes and it was obvious there was a strong feeling that Cuyahoga County citizens should have a medical care plan, these physicians as individuals assumed leadership in that direction. The purpose of the plan is "to establish, maintain, and operate a voluntary, nonprofit medical care plan within the limits of Cuyahoga County whereby professional service will be provided to such persons as shall become subscribers to such plan." The most recent medical care plan worked by the economics committee, approved by the academy directors and rejected by the members of the academy, will be used as a working basis after incorporation, it was stated. The plan will probably be checked by state insurance and medical boards. Then, according to law, it will have to receive the support of 51 per cent of physicians residing in and actively practicing in the county. How Cleveland physicians now in military service will figure in the plan is another technicality which will have to be ironed out, it was said.

OREGON

Society News.—Physicians and dentists of Klamath and Jackson counties met jointly with the Southern Oregon Medical Society, June 13, to hear, among others, Dr. Leo Eloesser, San Francisco, discuss "Treatment of Compound Fractures in War Time" and Henry Cline Fixott, D.M.D., Portland, "Planigraphy of the Teeth and Head."——Dr. Eugene R. Kellersberger, New York, spoke on "Tropical Diseases" before the Multnomah County Medical Society, Portland, April 24.

Personal.—Ralph E. Jackson, Salem, former claim supervisor of the Oregon State Industrial Accident Commission, has been named general manager of the Multnomah Medical Service Bureau. This is the first time the bureau, which carries the approval of the state medical society and the Multnomah County Medical Society, has employed a full time general manager.——Dr. Harold B. Stout, formerly of Pateros, Wash., has been appointed health officer for Douglas County. ——Florence Peebles, Ph.D., since 1935 professor of biology at Chapman College, Los Angeles, has been appointed director of the biologic laboratory of Albany College, Portland.

PENNSYLVANIA

District Meeting.—The Eighth Councilor District of the Medical Society of the State of Pennsylvania was addressed in Conneaut Lake, July 15, among others by Drs. Irwin M. Pochapin, Pittsburgh, on "Medical Aspects of Chemical Warfare" and Roy R. Snowden, Pittsburgh, "Recent Advances in Our Knowledge of Hypertension." On behalf of the state society Dr. Walter F. Donaldson, Pittsburgh, secretary of the state society, presented fifty year testimonial certificates to Drs. Robert W. Brown, Greenville; John F. Rutherford, Hastings, and Owen M. Shreve, Erie.

Philadelphia

Personal.—George W. Patterson, P.D., assistant professor in bacteriology and director of athletics, Philadelphia College of Pharmacy and Science, has been elected president of the Alumni Association of the college. Dr. Jack I. Feinman has been appointed a member of the teaching staff, succeeding Dr. Edward A. Mullen, assistant professor in pharmacology, now on leave of absence and serving as commander in the U. S. Navy.

TEXAS

University and Foundation Cooperate in Medical Center.—An agreement between the Southwestern Medical Foundation and Baylor University to set up a medical center in Dallas was approved at a special meeting of the executive board of the Baptist General Convention on July 7. The project has been under consideration for eight months. Under a ninety-nine year contract the medical and dental schools of the university will be moved, as soon as buildings are provided, to a 35 acre tract along Hines Boulevard and including Parkland Hospital. Under the contract one million dollars will be expended by the foundation for buildings for medical teaching, construction to start within a period of not less than two years after removal of priority restrictions. Parkland Hospital will be enlarged and become an integral part of the center, its facilities to be used in connection with the medical and dental colleges. The site for the center is within a few blocks of a large group of children's hospitals, including the Children's Hospital of Texas, the Scottish Rite Hospital for Crippled Children, Hope Cottage, Bradford Memorial Hospital for Babies and Freeman Memorial Clinic. The agreement places the two schools under the control of a joint board including three members from the foundation and two from Baylor. The university, which has been under super-

vision of the executive board of the Baptist General Convention, will be conducted on a nonsectarian basis. Development of the medical center will be in cooperation with the city-county hospital board administering Parkland Hospital, where the first aim of the medical foundation will be to improve clinical facilities. A dispensary will be the first unit in the new construction program. In addition to providing the buildings, the foundation will also furnish money for teaching. The medical school will continue to receive income from endowment, but Baylor University will retain the endowment fund. All student fees will go into the fund for teaching.

WISCONSIN

Full Time Tuberculosis Secretary.—Dr. Oscar Lotz, Milwaukee, since 1939 part time executive secretary of the Wisconsin Anti-Tuberculosis Association, has been appointed to a full time basis. Dr. Lotz has been serving on a part time basis since the death of Dr. Hoyt E. Dearholt, for many years secretary of the association. He plans to give up his private practice.

Physician Observes Ninety-Sixth Birthday.—Dr. John G. Meachem, Racine, a life member of the State Medical Society of Wisconsin, recently celebrated his ninety-sixth birthday. Dr. Meachem graduated at Rush Medical College in 1865. For many years he served as a member of the municipal board of health of Racine. In 1932 he donated a chapel and library to St. Luke's Hospital, Racine, of which he with his father, Dr. John G. Meachem Sr., was one of the incorporators. The chapel is a memorial to his wife, and the library commemorates three generations of his family, who have been physicians. His son, Dr. John G. Meachem III, died in 1926.

Society News.—The Milwaukee County Medical Society was addressed on May 8 by Drs. Walter P. Blount, Milwaukee, and Philip S. Hench, Rochester, Minn., on "The Kenny Treatment of Poliomyelitis" and "The Management of Rheumatoid Arthritis" respectively.——Dr. John E. Gonce Jr., Madison, discussed "Some Aspects of Urinary Infections in Infants and Children" on May 21 before the Racine County Medical Society.——At a joint meeting of the Winnebago County Medical and Dental societies on May 7 in Oshkosh Dr. Kenneth W. Penhale, Chicago, spoke on "Traumatic Injuries to the Face."——Dr. Philip Levine, Newark, N. J., discussed "Isoimmunization, Practical and Theoretical Considerations," before the University of Wisconsin Medical Society in Madison recently.

GENERAL

Grants for Research on Infantile Paralysis.—The National Foundation for Infantile Paralysis, Inc., has given a total of $325,844.25 to twenty-six institutions in the United States and Canada to carry on virus and after-effect research work and education in the campaign against infantile paralysis. The funds were taken from the proceeds of the foundation's programs observing the President's birthday. The grantees and the amount of each grant follows:

For After-Effects Research

State University of Iowa College of Medicine, Iowa City	$11,200.00
University of Rochester School of Medicine and Dentistry, Rochester, N. Y.	9,200.00
University of California Medical School, San Francisco	5,050.00
The Children's Hospital, Boston	4,250.00
Massachusetts General Hospital, Boston	4,200.00
Michael Reese Hospital, Chicago	3,000.00
University of Toronto School of Hygiene, Toronto, Canada	1,000.00
New York Society for the Relief of the Ruptured and Crippled, New York	1,000.00
University of Southern California School of Medicine, Department of Anatomy, Los Angeles	890.00

For Virus Research

The Johns Hopkins University, Baltimore	59,244.00
University of Michigan, School of Public Health, Ann Arbor	40,000.00
University of Minnesota Medical School, Minneapolis	13,255.25
Michigan Department of Health, Lansing	13,210.00
University of Wisconsin, Madison	12,200.00
Connaught Laboratories, University of Toronto, Toronto, Canada	10,860.00
University of Michigan, Ann Arbor	7,000.00
University of Chicago, Chicago	6,090.00
Wayne University College of Medicine, Detroit	4,700.00
National Institute of Health, Bethesda, Md.	3,500.00
University of Pennsylvania, Philadelphia	2,500.00
Harvard Medical School and Surgical Research Laboratory, Boston City Hospital, Boston	1,500.00

For Education

Georgia Warm Springs Foundation, Warm Springs	50,120.00
National Organization for Public Health Nursing, New York	31,100.00
National League of Nursing Education, New York	16,000.00
Harvard Infantile Paralysis Commission, Boston	5,000.00
Frances Payne Bolton School of Nursing, Western Reserve University, Cleveland	9,775.00

FOREIGN

Public Health Under Hitler's Rule.—A few hundred cases of smallpox were verified recently in Paris, and those engaged in public positions have been required to be vaccinated, according to the *Göteborgs Handels- och Sjöfarts-Tidning* of April 7. French physicians unanimously state that illness is much more prevalent in France as a result of the present dietary restrictions. An increase has occurred in the number of operations for hernia, nephroptosis and organic disorders peculiar to women, owing, it is said, to the loss in weight and the consequent reduction in fatty tissue which normally holds the organs in their proper position. Fractures of bones have been extremely common, especially in old people who are not getting enough calcium, phosphorus and vitamin D in their food to maintain adequately the bone structure. More cases of rickets are being reported. Convalescence following operations is delayed. Many surgeons complain that operative wounds do not heal as readily as formerly, they have difficulty in stopping hemorrhage following operations, infections are more common because of lack of antiseptics, operating rooms cannot be adequately heated and bandage material is getting low.

According to the *Berliner Borson-Zeitung* of April 24, the general picture in public life is one of nervousness and short temper. Everywhere, it is said, one has to witness rows. To appreciate the meaning of politeness one need only witness how the fuehrer receives and takes leaves of his guests at his front door.

The *Mir* of Sofia, April 15, stated that the Directorate of National Health has ordered that all products used as substitutes for coffee or tea, such as soya beans, chick-peas, almonds and carrots, must be sold under their proper names and that it is forbidden to use the word "substitute."

J. Lhost in *Le nouveau journal*, April 21-22, writes about the housing conditions: "In addition to the fits of nostalgia suffered by the Belgian workers in Germany, there is the more or less comfortless home life which they endure. The reich is suffering from a great lack of housing accommodation. Circumstances have not permitted the construction of suitable houses to be carried out on the same scale as the terrific influx of foreign workers. The present conflict has interrupted Hitler's plan for the erection of workmen's dwellings, and the Germans themselves find it difficult to obtain accommodation. In order to satisfy the most pressing needs the Germans have had hurriedly to put up provisional barracks and in some of the larger towns to commandeer whole hotels to furnish lodgings for the workers. These emergency measures and overpopulation have resulted in a sort of local bottleneck the result of which is an unpleasantly crowded communal life, collective kitchens and a kind of intermittent camp life. Such drawbacks are not very serious in themselves, and the workers do not exaggerate them; but, taken in conjunction with the effects of the general nostalgia, they produce results which the German labor front is doing everything in its power to avoid."

Government Services

Course in Occupational Dermatoses at National Institute of Health

The U. S. Public Health Service will give a course in occupational dermatoses at the National Institute of Health, Bethesda, Md., stressing the war industries, July 27-August 8. The course will consist of six days of lectures, four hours daily, and six days of visits to six plants which manufacture war materials. The number of applications received for taking the course completely fills this present class, but if there is a demand from a sufficient number of dermatologists it is possible that another course may be given. Applications for the course should be sent to Dr. Louis Schwartz, medical director, Dermatoses Investigations Section, National Institute of Health, Bethesda, Md.

CORRECTION

Dr. Arbor D. Munger.—In THE JOURNAL, July 4, page 812, second column, third line from the bottom, the name Dr. Arthur D. Munger, Lincoln, Neb., should have been Dr. Arbor D. Munger, Lincoln, Neb. At the June 12 meeting of the Section on Urology of the American Medical Association, Atlantic City, Dr. Munger was elected vice chairman of the section.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 13, 1942.

Lives Saved by Iron Table Shelters

The latest form of shelter against bombing is an iron table capable of sustaining many tons. In a recent raid the value of the shelter was shown by the escape of an adult and two children in a home demolished by a direct hit. This occurred in spite of the fact that the shelter was hurled 46 feet over an outdoor shelter and into a first floor room of another house. When assisted from the shelter the adult and one child were found to be injured and were taken to a hospital, where they are recovering. The other child was unhurt. In another case, as the result of a direct hit, the débris of a two story building completely buried a table shelter on the ground floor. When rescuers arrived five persons were helped out, shaken but uninjured. In a third case in which the house was demolished, the shelter was lifted sideways 6 feet and upward 4 feet onto débris. The shelter held four persons, who were unhurt. A report of the experts of the Ministry of Home Security on thirty-nine bombing incidents in which the table shelters were involved shows that they have stood up well to severe tests. Of one hundred and nineteen persons in these shelters only four were killed, seven were seriously injured, fourteen were slightly injured and ninety-four escaped uninjured.

Casualties of the British Empire in the First Two Years of the War

In the House of Commons Mr. Attlee, secretary of state for the dominions, gave the casualties in the armed forces of the British Empire from Sept. 3, 1939 to Sept. 2, 1941 (excluding deaths from natural causes) as:

	Officers	Other Ranks	All Ranks
Killed	6,296	42,677	48,973
Wounded	4,064	42,299	46,363
Prisoners of war	3,374	55,084	58,458
Missing	953	28,803	29,756
Total	14,687	168,863	183,550

New System for Hospital Outpatients

Before the war the need for a scheme to curtail the long period of waiting for patients attending the outpatient department of Guy's Hospital was recognized. The fact that many of these patients are now engaged in work of national importance and can ill afford to wait long hours has made the problem urgent. Under the previous system the waiting period extended to three or four hours. A new system has been introduced under which appointments are made in hourly blocks, so that one batch of patients attends from 9:30 to 10:30, the next from 10:30 to 11:30 and so on. Thus no patient has to wait more than an hour and many much less. The number of patients booked for each hour varies in different clinics. It has been found that physicians deal with 2 to 4 new cases an hour or 8 old cases, but surgeons see 6 new cases an hour. An unavoidable disadvantage of the scheme is that patients who are booked may fail to attend and make a gap in the sequence of cases. This sometimes can be filled by other patients, but on occasions the physician has to wait for the next patient. On the whole the new scheme has proved advantageous. It relieves the congestion of the outpatient department and succeeds in its main object of relieving the waiting period. It permits the nurse to prepare more efficiently for the management of the session.

The Head Louse and Modern Hairdressing

The managing director of a well known firm of hair dressers has written to the *Times* suggesting that, contrary to common belief, permanent waving is conducive to hair hygiene and elimination of the head louse. This led to a reply from Kenneth Mellanby of Sheffield University, who recently made a report of an investigation, undertaken on behalf of the Board of Education and the Ministry of Health, into the incidence of the head louse. He wrote "Modern styles of hairdressing are, unfortunately, likely to favor an increase of the number of head lice. I have heard of frequent cases of young women with long permanently waved hair which is apparently never disturbed for weeks and which forms an ideal breeding ground for parasites." He has since learned that the reason these women do not comb their hair is not the permanent wave. Two processes are involved in producing an elaborate coiffure. First, if the hair is straight its structure is deformed to produce a result like natural waviness. This change is permanent and will survive brushing and washing. The second process consists in "setting" the hair, which may be arranged in any type of bizarre confection. This "set" is a delicate structure easily disturbed, and its production requires time, patience and skill. Mellanby says that the hairdressers will do much to reduce the incidence of the head louse if they can persuade women to avoid elaborate "sets," which, because of the difficulty of replacing them, are often left uncombed and unwashed for long periods. Further, the shorter the hair the less liable it will be to louse infestation.

Effects of the War on Human Fertility

The birth rate has fallen to a level which in the near future means a decline of population. The number of persons in this country between the ages of 14 and 64 is 33 million, and two thirds of them are engaged in the war effort, whether in the armed forces, civil defense or war industries. No country has ever before mobilized its man power to the extent we have. The effect of the war on the birth rate is interesting. Except as it causes a temporary loss of births by separation of man and wife and a permanent loss of potential fathers and mothers by violent deaths, it seems that the war may have a favorable effect on fertility in the long run by bringing about a change in values and removal of some of the deterrents to childbearing. There has been a remarkable increase in marriages. This is in part due to the large number of girls reaching the ages of 19 and 20 owing to the high birth rate which followed the last war. But more important are the allowances provided for the wives of the fighting men. The birth rate for the first quarter of 1942 was higher than for any other first quarter since 1931, in spite of the disruption of family life produced by the war, including the bombing of our cities and their evacuation on a large scale.

Demand for Further Measures in Prevention of Venereal Diseases

At a meeting of the Medical Society for the Study of Venereal Diseases a discussion on the need for further powers to deal with sources of infection, contacts and defaulters was opened by Major S. M. Laird. He pointed out that now any person is free to have venereal disease and to communicate it as much as he chooses and is not obliged to be treated or to continue treatment until cured or rendered noninfectious. He is under no obligation to assist in tracing his infective consort, who is free to refuse examination and treatment. In the absence of notification no accurate knowledge of the incidence of these diseases exists. Control is prevented in this country by three factors—technical imperfection of the medical profession, the defaulting patient and the untraced sources of infection and their contacts. Venereal diseases should be dealt with only

by practitioners who have successfully passed through postgraduate instruction in them. The defaulter rate is high; in 1935 only 17.5 per cent of patients completed treatment and tests of cure at the treatment centers. The corresponding figure for Sweden was 97.5 per cent. The New York commission which in 1936 studied antivenereal methods in Britain and Scandinavian countries reported in favor of the compulsory powers in use in the latter. The cases of syphilis reporting for the first time in Stockholm in 1935 were only 5 per cent of those in 1919. In Liverpool the corresponding figure was 37 per cent. The British minister of health should without delay arrange for survey of the venereal disease problem in this country with a view to a trial of notification and compulsory measures. There was also need for intensive education of the public as to venereal diseases.

In the discussion there was general agreement as to the demand for compulsory powers. The resolution was passed unanimously "that in the opinion of this meeting of the Medical Society for the Study of Venereal Diseases further measures, legislative and administrative, in the treatment and prevention of venereal diseases are required to deal with defaulters, sources of infection and contacts."

The Collection of Medicinal Plants

Before the war we imported most of the medicinal plants we required, as we did most of our food and of many other things. But the need to devote as much shipping as possible to purposes of the war has compelled us to develop and use our home resources. In normal times many hundreds of tons of medicinal plants which could be gathered from the countryside were imported. Even such common plants as dandelions and stinging nettles were imported for the manufacture of drugs. This year the collection of medicinal plants is being organized on wide lines. Herb committees have been set up in forty-eight counties to arrange the collection, drying and dispatch to the manufacturers. Schools and youth organizations are helping in the collection. Among the wild herbs now being collected are buckthorn, red poppy petals, elder flowers, comfrey, coltsfoot, horse radish, hyssop, hemlock, henbane, foxglove, dandelions and stinging nettles.

The Immunization of Children Against Diphtheria

The Ministry of Health has issued a memorandum drawing attention to an increase in the dosage of alum precipitated toxoid for the production of artificial immunity against diphtheria which experience has shown to be desirable. At the end of 1940 the ministry undertook to provide gratuitously this prophylactic. The laboratories responsible for the distribution were informed that as a result of large scale trials a Schick conversion rate of about 98 per cent had been obtained with two doses of 0.1 and 0.3 cc. respectively at an interval of not less than four weeks. This dose was generally adopted. But it was soon found that one preparation of alum precipitated toxoid, though satisfying the regulations, yielded a much lower Schick conversion rate than 98 per cent and its issue was stopped. Further tests showed that the unsatisfactory results were not due to small doses employed but to a fundamental defect in antigenic potency.

It has been realized for some time that the assessment in the laboratory of the antigenic potency of alum precipitated toxoid presents considerable difficulty and that the tests laid down by the Therapeutic Substances Act may need revision. A more satisfactory method of preparing alum precipitated toxoid has recently been published and is available to all manufacturers. Tests carried out with the product have yielded satisfactory results with a dose of 0.1 and 0.3 cc. at four to six weeks' interval. Nevertheless certain considerations suggest an increase of the dose to widen the margin of safety. Therefore it is recommended that doses should be raised to 0.2 and 0.5 cc. The increase in the first dose is recommended mainly on practical grounds. The full quantity of antigen may not be introduced owing to an imperfectly calibrated syringe or to an escape of some of the inoculum. Another reason may be lack of uniformity of the inoculum, owing to neglect to shake the bottle thoroughly or to sedimentation in inoculating successive children. In issuing this memorandum the ministry takes the opportunity to emphasize that the immunization of children between the ages of 5 and 15 years will not alone suffice to reduce materially the incidence of diphtheria. This can be achieved only if a majority of the children of preschool age also are immunized. Children thus protected early should receive a supplementary dose of 0.5 cc. on beginning school life.

Mass Radiography for the Detection of Tuberculosis in Recruits

The minister of labor and national service has presented to Parliament a report of his medical advisory committee, of which Lord Horder is chairman, on mass miniature radiography in the detection of pulmonary tuberculosis in recruits for the services. Requests were made by the National Association for the Prevention of Tuberculosis and by the Standing Advisory Committee on Tuberculosis that this method should form a normal part of the examination of recruits. Some two hundred recruits can be dealt with in an hour, but the photographs must afterward be processed and interpreted by tuberculosis specialists. The committee has no doubt of the value of the method and repeats an opinion previously expressed that its addition to the clinical examination of all recruits and to the radiologic examination by specialists of suggestive cases would be ideal. But for various reasons it is not practicable. The medical examination of recruits is done at two hundred centers and there are neither the machines nor the staffs available for all these boards.

The best alternative would be radiologic examination to the greatest number practicable after entry into the services, when recruits can be concentrated for the purpose at suitable depots. The committee commends steps already taken in this direction. The navy has examined many thousands by mass radiography, and active pulmonary tuberculosis was discovered in 0.3 per cent. The naval experience shows that it is far more important to examine trained men than recruits, as the majority of nonsymptomatic carriers of tubercle bacilli are found after they have been some time in the service rather than at the time of joining. In the air force the percentage of tuberculous found after joining was 0.2 and in the army 0.1. Measures already adopted by civilian medical boards have resulted in the rejection of about 1 per cent on account of pulmonary tuberculosis. This corresponds roughly with what is believed to be the incidence in the general population. The experience of the service examinations is that the number of cases of tuberculosis which the civilian boards failed to detect is between 1 and 2 per thousand. Thus the problem is of small magnitude.

Cancer Research

The eighteenth annual report of the British Empire Cancer Campaign deals with the carcinogenic activity of many new synthetic compounds. British laboratories have led the way in the study of cancer producing and cancer inhibiting substances. In the research institute of the Cancer Hospital a research has been undertaken on seventy compounds, mostly new chemical substances synthesized for the purpose. The results support the view that there is an association between molecular structure and carcinogenic action. An attempt has been made to determine the occurrence of carcinogenic factors in the body. By subcutaneous injection of extracts of human liver, obtained from cases of cancer, seventeen sarcomas have been produced

in mice. Attempts are being made to identify the active constituent of these extracts. The results so far obtained are difficult to interpret but form an encouraging basis.

The possibility that wood smoke, much used for food preservation, might contain carcinogenic substances has been investigated at the Cancer Research Laboratory, Newcastle-upon-Tyne, with negative result. At the Oxford University research center of the campaign investigations have been carried out on the striking augmentation of carcinogenesis when croton oil acts on mouse skin in conjunction with a dilute solution of benzpyrene. This effect has been traced to a croton resin in the oil. It has also been shown that this resin can convert a preneoplastic into a neoplastic lesion. The fact that this can be brought about by substances not themselves carcinogenic may have important clinical implications.

The clinical cancer research committee of the campaign is investigating the records of 15,000 cases. This year uterine cancer is the object of detailed study. Dr. Percy Stocks of the General Register Office has made some interesting observations on the statistical significance of these returns. The liability to cancer of the cervix is greater at every age among married and widowed than among single women, especially between the ages of 45 and 65, when it is about seven times as great. But liability to cancer of the corpus uteri is somewhat less among married and widowed women than among single women. Only 26 per cent of patients suffering from uterine cancer consulted a physician within the first month of noticing the first symptoms, and only 45 per cent within the first three months. In 75 per cent of the cases the physicians made an examination promptly and referred the patient to the hospital.

IRRADIATION OF MALIGNANT TISSUES

The reaction of normal tissues following irradiation by surface doses of the order of 300 to 400 roentgens per minute was found to be less intense than from the same quantity and quality of radiation given at a dosage rate of 20 roentgens per minute. But the reactions of malignant tissue to high intensity was earlier and greater than that produced at lower dosage rates. The enforced use of radon for radium has raised the question whether the same physical dose of the gamma rays has the same biologic effect. No difference could be found experimentally or clinically. At St. Bartholomew's Hospital work is being done with the million volt apparatus. A difference from the results of treatment of cancer of the rectum treated with the 200,000 volt apparatus is that temporary disappearance of the growth was more often observed.

A Register of Civilian War Dead

The Imperial War Graves Commission, which was established after the last war to take care of the graves of the many thousands of killed, has in this war made contact with the relatives of 67 per cent of the civilian war dead. Of these forty-two thousand were killed in Britain from the beginning of the war to the end of September 1941. The commission has obtained personal details for inclusion in a register which is being prepared. In order to make this as complete as possible a special appeal is being made to relatives or friends who have not replied to the commission's letter. The value of a personal communication was shown when a man from the East End of London called after receiving the usual letter concerning his daughter. He was able to supply details of more than twenty members of his family who had been killed. The ages of the civilian war dead range from 11 hours to 100 years.

University Adopts Health Tests for Students

As previously reported in THE JOURNAL, the routine medical examination of the young on leaving school, particularly x-ray examination of the chest for the detection of tuberculosis, is advocated. This procedure has now been adopted at one university, that of Sheffield. At first the examination was optional and the number of students who availed themselves of it was small—not more than 20 per cent. It has now been made compulsory. In other faculties than medicine it will not include x-ray examination of the chest. The medical student will not only undergo radiologic examination of the chest on entrance but have a second one, with a sedimentation test, when he begins his clinical work, and a third one at the end of his second clinical year. The object of this repeated examination of the chest is not only to benefit the student but to prevent him from conveying infection to the patients with whom he will be in contact.

New Portable Machine for Administering Anesthetics

The first two hundred machines which will simplify emergency operations in the field and in air raids was presented by Lord Nuffield, the automobile magnate, to the director general of Air Force Medical Service. The machine is the Oxford vaporizer which, contained in a vermin proof case about the size of a portable phonograph, will take the place of the cumbersome gas cylinders formerly used to administer anesthetics. In future a medical officer carrying this small case, which weighs 30 pounds, and a small bottle of liquid ether will have all the anesthetic equipment he needs. The vaporizer is the result of several years' research in the Nuffield Department of Anesthetics at Oxford University under the direction of Group Captain R. R. Mackintosh.

Liquid ether is vaporized inside the machine, and the patient inhales the gas. The vaporizer is foolproof and can be worked by any one with expert direction. In hot climates anesthetics evaporate as soon as they are poured on the face mask, often before the patient has time to inhale them. The vaporizer does away with this difficulty. Special experiments are being conducted with sand from the Libyan desert, so that filters can be fitted to prevent sand from affecting the machine.

Decree of Nullity of Marriage Obtained by Blood Test

For the first time in this country a blood test has been used in the law courts to disprove paternity. On June 15, 1940 a man cohabited with a woman, who told him a few days later that she was pregnant. He married her in August and left her soon afterward. On Jan. 8, 1941 she bore a full term child. Medical evidence established that the child could not possibly have been conceived in the previous June. The husband sued for a declaration of nullity of marriage on the ground that the woman was pregnant by another man at the time of the marriage. Dr. G. Roche Lynch, the government analyst, gave evidence that he had grouped the blood of the husband, wife and child. The husband's was OM, the wife's BM and the child's ABN. Therefore the factors A and N in the child's blood were not accounted for and the husband was not the father. The judge declared that the husband's case was clearly proved and pronounced a decree of nullity of the marriage.

Marriages

WILLIAM MASSIE SMETHIE, Richmond, Va., to Miss Avis Lee Harrington of Rocky Mount, N. C., in Chapel Hill, N. C., April 4.

HILTON DRUMMOND HAINES, Greenwich, Conn., to Miss Martha Ledbetter of Rockingham, N. C., April 25.

GUY HEWITT BRANAMAN, Waynesboro, Va., to Miss Merle Virginia Ferrell in Ronceverte, W. Va., April 18.

HENRY ST. GEORGE TUCKER JR., Richmond, Va., to Miss Mary Grasty Bell of Staunton, April 25.

GERALD WATTS SCURRY, Columbia, S. C., to Miss Emily Jordan Thomas in Charleston in April.

CHARLES W. HOCK to Miss Margaret Henley, both of Winston-Salem, N. C., April 30.

LEE BRAYTON, Indianapolis, to Miss Louise Kaup of Taylorville, Ill., April 4.

Deaths

Leon Kahn Baldauf, Waltham, Mass.; Johns Hopkins University School of Medicine, Baltimore, 1905; member of the Massachusetts Medical Society and the American Association of Pathologists and Bacteriologists; professor of pathology at the Middlesex University School of Medicine; at one time professor of pathology and bacteriology at the University of Louisville (Ky.) School of Medicine; formerly on the staff of the Cambridge City Hospital; aged 64; died recently in the New England Baptist Hospital, Boston.

William Aubrey Poole ✠ Lexington, Ky.; St. Louis University School of Medicine, 1906; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; past president of the Henderson County Medical Society; major in the medical corps of the U. S. Army during World War I; at one time health officer of Henderson; aged 60; died, June 2, of injuries received in an automobile accident in March.

Elmer Douglas Osmun, Allegan, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1892; member of the Michigan State Medical Society; served in the medical corps of the U. S. Army during World War I; for many years served on the board of education and as county coroner; examiner for the Selective Service System; aged 73; died, April 23.

Howard Kenneth Glidden, Swampscott, Mass. (licensed in Massachusetts in 1899); veteran of the Spanish-American War; formerly member of the board of health of Swampscott and school committee; aged 67; died, May 30, in the Massachusetts General Hospital, Baker Memorial, Boston, of heart disease, hypertension and arteriosclerosis.

Louis Dorpat, Milwaukee; Milwaukee Medical College, 1905; member of the State Medical Society of Wisconsin; formerly deputy state health officer; health officer of Ironwood, Mich., from 1924 to 1931; formerly superintendent of the South View Hospital; aged 70; died, May 25, in the Milwaukee County Hospital of coronary occlusion.

John Henry Ramey, Rock Camp, Ohio; Miami Medical College, Cincinnati, 1897; president of the board of education of Lawrence County; served in the medical corps of the U. S. Army during World War I; aged 69; died, May 28, in the Lawrence County General Hospital, Ironton, of left bundle branch block.

Carl Gustav Fahndrich ✠ Battle Creek, Mich.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1920; member of the American College of Chest Physicians; medical director of the Calhoun County Public Hospital; aged 47; died, May 31, in a hospital in Chicago.

Andrew Cornelious Dorminy, Hoboken, Ga.; Atlanta College of Physicians and Surgeons, 1911; member of the Medical Association of Georgia; also a druggist; served during World War I; aged 61; died, March 19, in the Veterans' Administration Facility, Lake City, Fla., of cirrhosis of the liver.

George Washington Billig ✠ Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1898; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; on the staff of Swedish Covenant Hospital; aged 65; died, June 7, of cerebral hemorrhage.

Arthur Lell Leeds, Phoenix, Ariz.; Hahnemann Medical College and Hospital, Chicago, 1902; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; for many years associated with the Indian Service; aged 72; died, May 7, of aneurysm of the aorta.

Frank M. Tracy, Kansas City, Kan.; College of Physicians and Surgeons, Medical Department, Kansas City University, Kansas City, 1899; formerly county coroner and member of the city council; aged 84; died, May 3, in St. Margaret's Hospital of coronary sclerosis and hypostatic pneumonia.

Gavin Hamilton, Houston, Texas; McGill University Faculty of Medicine, Montreal, Que., Canada, 1894; fellow of the American College of Surgeons; formerly on the staffs of the Memorial and Hermann hospitals; aged 70; died, May 26, of heart disease.

Gustus Brinton Hepp, Denver; Northwestern University Medical School, Chicago, 1891; member of the Colorado State Medical Society; on the staffs of St. Luke's, St. Joseph's and St. Anthony's hospitals; aged 76; died, May 26, of cerebral hemorrhage.

Thomas B. Snoddy, Pala, Calif.; College of Physicians and Surgeons, Little Rock, 1911; for many years physician in the Indian Service; aged 65; died, May 1, in the Mercy Hospital, San Diego, of pneumonia, diabetes mellitus and tuberculous meningitis.

Horace Shaughnessy E. Root, New York; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1924; until recently was employed by a construction company in Honolulu, Hawaii; aged 40; died suddenly, May 5, of coronary occlusion.

William Thomas Harvell, Oakland, Tenn.; Memphis (Tenn.) Hospital Medical College, 1899; served during World War I; aged 66; died, May 6, in the Veterans Administration Facility, Memphis, of encephalomalacia of the occipital lobes.

William A. Cotton, Escanaba, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1889; member of the board of directors of the Pinecrest Sanatorium, Powers; aged 78; died, May 26, in St. Francis Hospital.

Edward LeRoy Barnett ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1899; formerly on the staff of the Hospital for Ruptured and Crippled; aged 68; died, June 7, of coronary thrombosis.

Philip Schmitt, Milwaukee; Jefferson Medical College of Philadelphia, 1883; member of the State Medical Society of Wisconsin; aged 82; died, May 26, in the Milwaukee Hospital of carcinoma of the left tonsil.

Bryant Hooper Trewyn ✠ Peoria, Ill.; St. Louis University School of Medicine, 1925; president of the local board of education; on the staff of St. Francis Hospital; aged 41; died, June 9, of heart disease.

Adolph Noha, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1890; member of the Louisiana State Medical Society; aged 80; died, May 29, of chronic nephritis and uremia.

Benjamin Victor Howard, Knoxville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1912; formerly member of the state board of nurses' examiners; aged 53; died, May 24, of coronary occlusion.

Henry Worst Sweigart, Lewistown, Pa.; University of the City of New York Medical Department, New York, 1890; member of the Medical Society of the State of Pennsylvania; aged 76; died, May 18.

George Chauncey Wrigley ✠ Sonora, Calif.; College of Physicians and Surgeons of San Francisco, 1909; served during World War I; aged 57; died, May 1, of a skull fracture received in a fall.

Alexander W. Burch, Lincolnton, Ga.; University of Georgia Medical Department, Augusta, 1889; for many years member of the board of education and city council; aged 76; died, April 17.

William Henry Weed Hinds, Milford, N. H.; Boston University School of Medicine, 1895; member of the New Hampshire Medical Society; aged 74; died, March 10, in Wilton.

Andrew Wesley McClennan, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1907; formerly on the staff of the Toronto Western Hospital where he died, May 9.

Harold J. Hoover, Grand Ledge, Mich.; Saginaw Valley Medical College, Saginaw, 1903; aged 67; died, May 4, of chronic nephritis, hypertension and angina pectoris.

George Clinton Kilgore, Gloucester City, N. J.; Baltimore Medical College, 1895; aged 73; died, May 11, of laryngeal carcinoma.

Charles Edward Windeler, Chicago; Medical College of Ohio, Cincinnati, 1900; aged 64; died, May 9, of organic heart disease.

DIED IN MILITARY SERVICE

Frederick Talmadge Rice ✠ Major, U. S. Army, retired, registrar at the new U. S. Army Hospital (Hoff General Hospital), Santa Barbara, Calif.; Hahnemann Medical College and Hospital, Chicago, 1907; entered the medical corps of the U. S. Army as a captain in 1920 and retired with rank of major in 1929 for disability in line of duty; served during World War I; recalled to active duty May 7, 1941; aged 61; was killed, May 7, in an automobile accident.

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act and in cases in which they refer to drugs and devices they are designated D. D. N. J. and foods, F. N. J. The abstracts that follow are given in the briefest possible form: (1) the name of the product, (2) the name of the manufacturer, shipper or consigner, (3) the date of shipment, (4) the composition, (5) the type of nostrum, (6) the reason for the charge of misbranding and (7) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Anti-Poison.—Anti-Poison Medicine Company, Springfield, Mo. Oct. 11, 1939. Composition: essentially extracts of plant drugs including an astringent, alcohol (12.1 per cent by volume), water and a trace of an ammonium compound. Misbranded because label falsely represented the product as an effective treatment and cure of chills, malaria, eczema, scrofula, cholera morbus, reptile and insect bites, rheumatism, lung hemorrhages, asthma, female troubles, la grippe, erysipelas, "blood poison of every description," tumorous cancer, stomach and bladder diseases and many other disorders. Further misbranded because represented to contain 20 per cent of alcohol and to be an anti-poison, antiseptic and "the best blood medicine on the market."—[*D. D. N. J., F. D. C. 304; November 1941.*]

Coston's 6 and 3 Herb Compound.—C. S. Coston, Lockwood, Tenn. Jan. 17, 1940. Composition: essentially plant drugs including a bitter (aloe), an alkaloid bearing drug, a laxative drug, a trace of sodium benzoate, sugar and water. Misbranded because falsely represented on the label to be a stomachic, diuretic and laxative and a remedy for stomach, liver, kidney, blood and nervous disorders, rheumatism and some other things.—[*D. D. N. J., F. D. C. 306; November 1941.*]

Deane's Adhesive Bandage.—Deane Plaster Company, Yonkers, N. Y. June 29, 1940. Misbranded because of following false and misleading claims in labeling: "First aid for minor cuts. Wounds . . . Apply the gauze pad directly over the wound . . . Will afford complete protection from the cut or wound," whereas specimen examined was found to be contaminated with viable micro-organisms. Further misbranded because label did not bear the name and address of the manufacturer, packer or distributor.—[*D. D. N. J., F. D. C. 320; November 1941.*]

Diabet-Tea.—Diabet-Tea Company, Scranton, Pa. Sept. 11, 1940. Composition: ground *hypericum perforatum*, commonly called St. John's wort. Misbranded because of false statement on label: "Nature's Food Diabet-Tea for Diabetes. The contents of this package has been carefully prepared for the use of those who suffer from diabetes" and because label did not bear the common or usual name of the drug which comprises the preparation.—[*D. D. N. J., F. D. C. 307; November 1941.*]

Dr. Seth Hart's Croup Syrup.—Parker Medicine Company, Athens, Ohio. Jan 8, 1940 Composition: essentially sugar, water, extracts of plant drugs and 3 per cent of alcohol. Not efficacious for coughs, croup, acute bronchitis, pleurisy or inflammation of the lungs as represented, and hence misbranded.—[*D. D. N. J., F. D. C. 311; November 1941.*]

Fru-Lax.—Fru-Lax Company, Chicago. Between April 8 and July 9, 1940. Composition: essentially purging tissues of cassia, senna leaf and carob bean. Misbranded because label falsely represented that it was not habit forming; that it would restore health and relieve ailments caused by poisons absorbed from the bowels; that it was an effective treatment of rheumatism, neuritis, stomach disorders, gallbladder trouble, headaches, catarrh, skin ailments, colds, hemorrhoids, high blood pressure and some other things; that it was an "ideal neutralizer" which would make the body disease-proof and that it possessed rejuvenating and restorative properties.—[*D. D. N. J., F. D. C. 340; March 1942.*]

Kotalko.—Kotalko Sales Company, New York. Feb. 20, 1940. Composition not stated. Labeled in part: "For the Scalp—Kotalko—For the Hair." Misbranded because misrepresented as to net weight of contents and because container was deceptive.—[*D. D. N. J., F. D. C. 315 November 1941.*]

Lenmar Company's Infra-Red Lamp.—Lenmar Company, Los Angeles. July 26, 1939. Description: a heating element screwed into a table type lamp base. Misbranded because label falsely represented the lamp as giving forth "healing rays from the sun" that "penetrate deep into the flesh, stimulating the nerves and causing greatly increased circulatory action, which destroys infections, rebuilds diseased tissue and promotes bodily health and vitality, will relieve suffering from asthma, neuritis, stiff swollen joints, sinus trouble and rheumatism . . . breaks up congestion indicated by acute pain and poor circulation . . . Women experiencing trouble at menstruation will find comforting relief by using this . . . Infra-Red rays are also very beneficial in the treatment of inflammation of the gall bladder, hysteria, nervous diseases, inflammation of the various bones, membranes and inflammation of the joints."—[*D. D. N. J., F. D. C. 299; November 1941.*]

Lightning Hot Drops.—Herb Medicine Company, Springfield, Ohio. Jan. 2, 1940 Composition: ether, chloroform and alcohol. Misbranded because ingredients present in smaller amounts than those declared on the label as: "Each fluid ounce contains 48 minims of chloroform, 48 minims of ether, alcohol 60% by volume."—[*D. D. N. J., F. D. C. 313; November 1941.*]

Maurice Le Bell's Formula No. 7.—Hollywood Formulas, Inc., Los Angeles. Sept. 11, 1940. Composition: tablets containing Irish moss, rhubard root, seaweed, parsley leaf, cranberry fruit and leaves resembling celery. Misbranded because of false statements on the label such as "As recommended by Hollywood's famous Dr. Maurice Le Bell, D. C., reducing specialist" and in booklet, " . . . instructions contained in this booklet are a vital part of your reducing program . . . simplified form of the famous reducing methods used by Dr. Maurice Le Bell, D. C., in his many years of private practice . . . "—[*D. D. N. J., F. D. C. 341; March 1942.*]

Miracle Lotion.—Martinsville Laboratories, Inc., Martinsville, Va. July 1, 1940. Composition: isopropyl alcohol, 60 per cent by volume, salicylic acid, benzoic acid, water, perfume and a green coloring material. Misbranded because label falsely represented that the product was good for scalp diseases, dandruff, falling hair and skin disorders in general, such as itch, ringworm and pimples, and, in addition, aching joints or muscles and some other conditions. Further misbranded because amounts of the ingredients not accurately declared on labeling nor was quantity, quality or proportion of alcohol correctly stated.—[*D. D. N. J., F. D. C. 298; November 1941.*]

Odell's Quinine for the Hair.—Odell Company, Newark, N. J. Nov. 19, 1940. Composition not reported. Misbranded because name falsely represented that the product contained quinine, which it did not; further misbranded because label did not bear common names of the active ingredients or a statement as to amount or proportion of alcohol present.—[*D. D. N. J., F. D. C. 297; November 1941; C. N. J., F. D. C. 60; January 1942.*]

Oster Massagett.—John Oster Manufacturing Company, Racine, Wis. Jan. 18, 1940. Description: "an electric motor so constructed as to vibrate when it revolved, and fitted with an attachment whereby it was clamped to the back of the hand." Misbranded because label falsely represented that this device would be efficacious for development and preservation of good health, stimulate blood circulation, eliminate congestion and banish localized pain; would give some relief in acute types of arthritis and delay the progress of chronic arthritis; would be of great value in the treatment of sprains and bruises by restoring the blood circulation, would ease stiff joints and separate adhesions therein; would penetrate deeply into the stomach and intestines with sufficient force to help normalize the natural functions of the digestive organs and be effective in mental fatigue, headache, nervousness, insomnia and nerve prostration and many other disorders.—[*D. D. N. J., F. D. C. 309; November 1941.*]

Purity Pine Disinfectant.—Wilco Laboratories, Inc., New York. Sept. 29, 1939. Composition: soap, water and pine oil. Misbranded because falsely represented in labeling as effective in the treatment of minor cuts and wounds.—[*D. D. N. J., F. D. C. 310; November 1941.*]

Samson Therapeutic Lamp.—Samson United Corporation, Rochester, N. Y. Between Nov. 25, 1939 and Jan. 2, 1940. Description: a table type lamp fitted with a heating element. Misbranded because of following false and misleading claims in accompanying circular: "Excellent for relief of arthritis, lumbago, cramps, colds, sprains, etc. . . . Designed by prominent engineers and approved by outstanding health authorities, this therapeutic lamp, used a few minutes daily, brings you health, beauty and vitality. Care of hair. General application of therapeutic rays every night will keep scalp healthy and improve blood circulation . . . Colds. Apply rays to back of neck and downward along spine to relieve congestion. Cramps . . . rheumatism . . . menstrual pains . . . insomnia . . . backache . . . skin ailments. Therapeutic rays stimulate pores, eliminate all impurities and strengthen tissues. Invaluable in treatment of acne, crow's-feet, dry skin, oily skin, wrinkles, blemishes, etc."—[*D. D. N. J., F. D. C. 300; November 1941.*]

Slendotabs.—Keneco Products, Elmira, N. Y. May 18, 1940. Composition: in each tablet, approximately ½ grain of phenolphthalein, in addition to a resinous drug such as leptandra resin, compounds of iodine equivalent to 0.088 grain of iodine per tablet and alkaloidal material including strychnine. Misbranded because falsely represented on label to reduce excessive fat effectively, to be a scientifically balanced weight reduction method and to help eliminate waste matter and accumulated poisons from the body; further misbranded because label failed to reveal the presence of strychnine or to declare the amount thereof, or to warn the user that the product might be dangerous to health, particularly in cases of appendicitis, and might cause skin eruption and dependence on laxatives.—[*D. D. N. J., F. D. C. 342; March 1942.*]

Wittone.—Wittone Sales Agency of United Distributors, Inc., Louisville, Ky. About May 1940. Composition: essentially a watery solution of epsom salt with almost negligible amounts of iron and ammonium citrate and the salicylate, phosphate and bicarbonate of sodium, with flavoring material. Misbranded because label falsely represented it to be efficacious for the health, to help one eat and sleep well and correct bilious spells, dizziness, headaches, sour stomach and some other disorders and keep the system free from impurities. Further misbranded because, among other things, the "tone" part of the Wittone name would give the false impression that the product acts as a tonic. Also misbranded because label did not warn against giving the product to children, to whom its use might be dangerous, or against frequent or continued use, which might establish dependence on laxatives.—[*D. D. N. J., F. D. C. 344; March 1942.*]

Correspondence

AVERAGE AGE OF PHYSICIANS AT DEATH

To the Editor:—The analysis of the statistics obtained from the obituary list of THE JOURNAL (Deaths of Physicians in 1941, editorial, June 13, p. 565) reminds me of an interesting finding gleaned from that section some time ago. Weekly review of that column never failed to arouse my curiosity as to the average age of the physicians whose deaths were reported at the top of the list compared to that of those at the bottom.

It seemed an unusual opportunity to determine what price success or probably, more correctly, prominence. From this information, the life span of the physicians who attained position and prestige could be compared to that of those who appear to have lived under less stress among their patients.

To satisfy this curiosity, our resident, Dr. Mortimer Camiel, averaged the age of the first and the last ten of each column of thirty successive issues of 1939. On compilation of these figures, we learned that the average age of those high in the list was 64.6 years, as against 69.3 years for the lowermost ten, a difference of 4.7 years.

RICHARD A. RENDICH, M.D., Brooklyn.

ARTERIOSCLEROSIS AND VARICOSE VEINS

To the Editor:—In the paper on arteriosclerosis and varicose veins by Drs. Lake, Pratt and Wright (THE JOURNAL, June 27, p. 696) appears the statement: "Although years of study by numerous workers have been devoted to this great enigma of biology, it can be fairly stated that today it is not known whether arteriosclerosis should be considered as a disease or as a purely degenerative process."

The arterial lesions that are discussed in this paper are largely due to atherosclerosis, after primary spasmodic processes and the minor Mönckeberg's sclerosis are excluded. Atherosclerosis is not a "purely degenerative process." It is a complex disease as specific in character as the infectious diseases. Unlike so-called senile sclerosis, a negative condition due to passive dilatation of weakness of arterial walls, atherosclerosis is an active disease of positive quality, which may even be characterized as an aggressive disease when it kills robust boys in the twenties with the highly selective process coronary sclerosis.

The only criteria that we have for demonstrating the causative relation of a given agent to a disease are Koch's postulates applied to infectious diseases. They require that the agent shall be found constantly in the lesions of the disease, shall be isolated in pure culture and shall reproduce the lesions of the disease when introduced into susceptible animals. We have been compelled to make compromises with Koch's laws in some infections because we cannot cultivate the suspected agent, or susceptible animals cannot be found, or for other reasons.

Cholesterol visible under the polariscope is normally limited to the adrenal cortex, myelin sheaths, interstitial testicular cells and sometimes corpora lutea. Visible cholesterol in other sites in the body is associated with disease. It is excess cholesterol. Ester cholesterol can be identified in the tissues by its specific crystals more readily than can bacteria. It has been demonstrated that excess cholesterol is an irritant comparable to a degree with silica. Visible cholesterol is always present in the lesions of atherosclerosis. It is the distinguishing mark of this form of arteriosclerosis. It can be extracted from the atherosclerotic lesions. When fed to rabbits in adequate dosage it will reproduce the lesions of human atherosclerosis with more exactness than can the lesions of many infectious diseases be reproduced by the introduction into susceptible animals of the accepted bacterial causes of these diseases (*Arch. Path.* **32**:507 [Oct.] 1941). No compromises with Koch's postulates are necessary in determining the causative relation of excess cholesterol to atherosclerosis.

Atherosclerosis, the important form of arteriosclerosis, is a specific disease due to excess cholesterol.

TIMOTHY LEARY, M.D., Boston.

"RADIATION THERAPY OF PROSTATIC CARCINOMA"

To the Editor:—In the able survey of the present day therapy in cancer of the prostate there appears to have crept into the Query and Minor Note of March 7 at least one inaccuracy. The author of the answer says "once the clinical diagnosis of carcinoma of the prostate has been made it is technically impossible to do any sort of surgical procedure that would effect a cure." As far as the surgical cure of this highly malignant disease is concerned, that has been answered by Drs. Hinman, Lowsley and Young in their communications of June 20. As far as irradiation goes I have reported two authenticated five year cures proved by pathologic specimen before treatment (by radon needles) and proved carcinoma free at autopsy five years later (*J. Urol.*, March 1942).

In the same article I reported that of 352 patients 21 (6 per cent) lived more than five years, apparently free from carcinoma for periods between five and nineteen years, 5 for five years, 6 for six years, 1 for seven years, 2 for eight years, 2 for nine years, 1 for ten years, 1 for twelve years, 1 for thirteen years, 1 for sixteen years and 1 for nineteen years. In but 10 of these cases was the diagnosis made pathologically. In 3 cases the diagnosis was by aspiration biopsy, and in 8 cases the diagnosis was made clinically.

Aspiration biopsy is a decided step in advance whereby to prove pathologically the presence of early carcinoma. This method, stressed for many years at the Memorial Hospital, has been largely neglected by urologists. It has proved in our hands a valuable method of diagnosis, not always succeeding, but when positive serving as an important means of early diagnosis.

Orchiectomy as advanced by Huggins marks a milestone in progress. He has shown that 5 out of 45 patients with advanced prostatic carcinoma with metastasis are apparently free from disease, the longest having gone some thirty-two months after this operation.

BENJAMIN S. BARRINGER, M.D.,
Memorial Hospital,
New York.

PURKINJE AND THE ORIGINS OF OPHTHALMOSCOPY

To the Editor:—To your editorial "Purkinje and the Origins of Ophthalmoscopy" in THE JOURNAL, May 23, page 348, I object that you spell Purkyně's name in three different ways: Purkinje, Purkině and Purkyně, the last one being correct.

John Evangelist Purkyně was born in 1787 in Bohemia of Czech parents and died in 1869 as a professor of the Charles University in Prague. He was the founder of the modern Czechoslovak medicine.

Although the American textbooks spell his name Purkinje, the correct spelling of his name is Purkyně and the correct pronounciation is Poor-ki-ne.

Otherwise I thank you for giving proper credit to my great countryman.

KAMIL JAROMIR NEUMAN, M.D., Schenectady, N. Y.

Council on Medical Education and Hospitals

CONTINUATION COURSES FOR PRACTICING PHYSICIANS

In accordance with the plan of the Council on Medical Education and Hospitals, advance information concerning continuation courses for practicing physicians available in the various centers is published quarterly. The following list consists of courses beginning during the period July 20-Oct. 20, 1942. It is hoped that this material will be useful to the practicing physician who is planning to take postgraduate work but does not have a ready means of knowing when and where the subjects in which he is interested will be taught. Since many of the classes are necessarily limited, those who contemplate enrolling in any of these courses are urged to communicate as early as possible with the proper executive officer.

H. G. WEISKOTTEN, M.D.,
Secretary, Council on Medical
Education and Hospitals.

Continuation Courses for Practicing Physicians, July 25-October 25, 1942

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
ALLERGY—See also Dermatology and Syphilology					
University of Pennsylvania Graduate School of Medicine	Arranged; 4 weeks, about 40 hours	.....	Individuals [1]	$150	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
ANATOMY—See also Gynecology, Orthopedics, Otolaryngology, Psychiatry & Neurology, Surgery					
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 60 hours	Applied anatomy of the ear, nose and throat	.....	$150 [2]	Dr. J. A. W. Hetrick, Dean, New York Medical College, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
	Arranged; 90 hours	Applied anatomy of pelvis and abdomen	.....	$250	
	Arranged; 60 hours	Applied anatomy of the urogenital system	.....	$150 [2]	
	Arranged; 100 hours	Surgical anatomy [3]	.....	$250	
ANESTHESIOLOGY					
Harvard University Medical School	Monthly; days and hours arranged	Clinical anesthesia	3	$30 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
Columbia University Faculty of Medicine	Any Monday when a vacancy occurs; full time for 2 or 3 weeks	General course	1 [1]	$100 [5] $150 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Arranged; 12 sessions	Regional anesthesia	2-4 [1]	$75 [5]	
New York Polyclinic Medical School and Hospital	1st of any month; 6 weeks or 3 months	General laboratory procedures; special courses arranged	4	Arranged	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
BACTERIOLOGY—See also Gastroenterology, Public Health					
Columbia University Faculty of Medicine	October; mornings for 1 month	Bacteriological service in medicine and surgery	5-20	$35 [5,6]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
BASIC SCIENCES—See Dermatology and Syphilology					
BIOCHEMISTRY					
Harvard University Medical School	Arranged	Research in biological chemistry	.....	Arranged [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
BRONCHO-ESOPHAGOLOGY—See Otolaryngology					
CARDIOLOGY					
Michael Reese Hospital	Aug. 17-29; full time for 2 weeks	Electrocardiography	.....	.....	Cardiovascular Department, Michael Reese Hospital, 29th and Ellis Avenue, Chicago, Illinois.
Harvard University Medical School	August; 6 mornings, 4 afternoons a week for 1 month	Combined course	10-20	$150 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
Tufts College Medical School	Sept. 28-Oct. 2, 1942	Electrocardiography		$25 [4]	Dr. Samuel Proger, Chairman, Postgraduate Department, Tufts College Medical School, 30 Bennet Street, Boston, Massachusetts
Columbia University Faculty of Medicine	Sept. 28-Oct. 2; Oct. 6-29; 9-5 daily	Electrocardiography	Minimum: 4	$50 [5,6]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 16 bi-weekly sessions	Clinical course	.....	$100	Dr. J. A. W. Hetrick, Dean, New York Medical School, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
University of Pennsylvania Graduate School of Medicine	Weekly; 5 days, about 30 hours	Electrocardiography and cardiac roentgenology	Individuals [1]	$60	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
CYSTOSCOPY—See Gynecology, Urology					
DERMATOLOGY AND SYPHILOLOGY					
Harvard University Medical School	Arranged; 2 mornings a week for 2 months	Clinical mycology	6	$30 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	October 1; [12] full time for 1 year	General course	Limited [7]	$300 [4]	
	Arranged; full time	General course Elective: Skin ward work	Limited [8]	Arranged [4]	
	Monthly; every morning	Practical course in dermatology	.....	$40 [4]	

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
DERMATOLOGY AND SYPHILOLOGY—Continued					
Columbia University Faculty of Medicine	Oct. 1, 1942-May 22, 1943	Basic sciences in their relation to dermatology and syphilology	Limited [1]	$75 [5,9]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	When a vacancy occurs; 6 weeks or 3 months	Clinical dermatology and syphilology	20 per section	$40 $75	
	When a vacancy occurs; 6 weeks or 3 months	Diagnosis and treatment of syphilis	6 per section	$25 [5] $40 [5]	
	Oct. 6, 1942-May 28, 1943	Pathological histology of diseases of the skin	Limited [1]	$75 [5]	
	When a vacancy occurs; 6 weeks or 3 months	Practical instruction in dermatologic allergy and immunology	3 [1]	$40 [5] $75 [5]	
	When a vacancy occurs; 6 weeks or 3 months	Practical instruction in diagnosis and management of syphilis	3	$40 [5] $75 [5]	
	Arranged; 6 weeks or 3 months	Practical instruction in minor dermatologic surgery	2 [1]	$40 [5] $75 [5]	
	Arranged; 6 weeks or 3 months	Practical instruction in mycology and animal parasitology as related to diseases of the skin	3 [1]	$40 [5] $75 [5]	
	When a vacancy occurs; 3 months, 6 months or 1 year	Practical instruction in pathological histology of diseases of the skin	12 [1]	$75 [5] $125 [5] $175 [5]	
	When a vacancy occurs; 6 weeks or 3 months	Practical instruction in physical therapy as applied to diseases of the skin	3	$40 [5] $75 [5]	
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time for 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
ELECTROCARDIOGRAPHY—See Cardiology					
ENDOCRINOLOGY—See Gynecology, Medicine					
ENDOSCOPY—See Gynecology, Surgery					
GASTROENTEROLOGY					
Columbia University Faculty of Medicine	Arranged; 2 months	Gastroscopy	Individuals [1]	$200	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 10 sessions	Gastroscopy	.....	$100 [10]	Dr. J. A. W. Hetrick, Dean, New York Medical College, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
	Arranged; 5 sessions	Peritoneoscopy	.....	$50 [10]	
Hahnemann Medical College	Arranged	Bacteriological technique	.....	Arranged	Dr. William A. Pearson, Dean, Hahnemann Medical College, 235 North 15th Street, Philadelphia, Pennsylvania
	Arranged	Duodenal-Biliary Drainage	.....	Arranged	
	Arranged	Gastroscopy		Arranged	
	Arranged	Intestinal Bacteriology	Individuals	Arranged	
	Arranged	Microscopy of Bile		Arranged	
University of Pennsylvania Graduate School of Medicine	Arranged; 16 weeks, about 500 hours	Clinical course	Individuals [1]	$400	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
GASTROSCOPY—See Gastroenterology, Otolaryngology					
GYNECOLOGY—See also Obstetrics, Pathology					
Harvard University Medical School	Oct. 1, 1942-Jan. 1, 1943; 12 or 25 exercises	Clinical gynecology	4 [11]	$25 [4] $50 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	August, September; [12] 1 month	General course	4 [11]	$75 [4]	
	Monthly; 10 exercises	Gonorrhea in women	3	$20 [4]	
Columbia University Faculty of Medicine	When a vacancy occurs; 15 sessions	Cystoscopy and endoscopy	6	$75 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Monthly; 10 sessions	Diagnosis and office treatment	6	$40 [5]	
	Monthly; 15 sessions	Diagnosis and office treatment	6	$60 [5]	
	Monthly; when class is formed; 8 weeks	Gynecological endocrinology	4 [9]	$100 [5]	
	Arranged; 4 weeks or more	Gynecological pathology	.....	Arranged [5]	

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
GYNECOLOGY—See also Obstetrics, Pathology—Continued					
	Oct. 5;[12] 1, 2 or 3 months	Seminar	4-6	$125 [5,6] $225 [5,6] $300 [5,6]	
	Monthly; Sept.-June; 4 weeks	Surgical anatomy as applied to operative gynecology	2-3 [4]	$200 [6]	
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course in gynecology and obstetrics	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
HEMATOLOGY—See also Surgery					
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 16 sessions	Physical diagnosis and hematology, especially in diseases of the thoracic organs	.....	$100	Dr. J. A. W. Hetrick, Dean, New York Medical College, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
INFANTILE PARALYSIS					
Georgia Warm Springs Foundation	July 20-25;[12] 1 week	Poliomyelitis during acute and convalescent periods	50 [13]	$25	Director, Graduate School of Physical Therapy, Warm Springs Foundation, Warm Springs, Georgia
University of Minnesota Center for Continuation Study	Sept. 21-26, Aug. 10-15	Kenny technic for management of acute phase	Limited [14]	$25	Dr. William A. O'Brien, Director, Department of Postgraduate Medical Education, The Medical School, University of Minnesota, Minneapolis, Minn.
LARYNGOLOGY—See Otolaryngology					
MEDICINE					
American College of Physicians	September 2 weeks	Allergy	Limited [40]	$40 [41]	E. R. Loveland, Executive Secretary, The American College of Physicians, 4200 Pine Street, Philadelphia, Pa.
	September 2 weeks	General course	Limited [40]	To be announced [42]	
	September 2 weeks	Internal medicine	Limited [40]	To be announced [42]	
Yale University School of Medicine: Connecticut Clinical Congress	Sept. 29-Oct. 1; daily	General subjects	.....	$2	Dr. Herbert Thoms, Secretary, Connecticut Clinical Congress, 789 Howard Avenue, New Haven, Connecticut
Harvard University Medical School	8-10 and/or 11 a.m. daily	Diabetes	Physicians welcome	None	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Aug., Sept.;[12] 5 days a week for 1 to 4 months	General course	.....	$150 [4] per mo.	
	Aug. 3-15	Selected subjects in endocrinology and metabolism	Minimum: 10	$80 [4]	
Tufts College Medical School	Oct. 5-30	Internal medicine		$50 [4]	Dr. Samuel Proger, Chairman, Postgraduate Department, Tufts College Medical School, 30 Bennet Street, Boston, Massachusetts.
Michigan State Medical Society	September	Institute: Practice of medicine in total war	Limited [43]	To be announced	Mr. William Burns, Executive Secretary, Michigan State Medical Society, 2020 Olds Tower, Lansing, Michigan
Kansas City South West Clinical Society	Oct. 5-8	Annual fall clinical conference		$5 [44]	E. Leas Clower, Executive Secretary, Kansas City South West Clinical Society, 208 Shukert Building, Kansas City, Missouri
Omaha Mid-West Clinical Society	Oct. 26-30; full time	Refresher course	.....	$5	Dr. J. D. McCarthy, Secretary-Director of Clinics, Omaha Mid-West Clinical Society, 1936 Medical Arts Building, Omaha, Nebraska
University of Buffalo School of Medicine	Sept. 21-26	Annual postgraduate course	.....	$5 per day	Dr. Frank Myers, Secretary, Committee for Postgraduate Courses, The University of Buffalo School of Medicine, 24 High Street, Buffalo, N. Y.
Columbia University Faculty of Medicine	Arranged	Medical statistics: Treatment of clinical and laboratory data	8	$30	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
	Oct. 12-16	Arthritis and allied rheumatic disorders	Minimum: 4	$35 [5,6]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Oct. 5;[12] 1 or 2 months	Seminar in internal medicine	4-10	$125 [5,6,10] $200 [5,6,15]	
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 9 sessions	Endocrine and metabolic disturbances, including diabetes mellitus	.....	$100	Dr. J. A. W. Hetrick, Dean, New York Medical School, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
New York Polyclinic Medical School and Hospital	Arranged; full time	Course for general practitioners	.....	$100	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
Duke University School of Medicine	1 week or more throughout the year	Practical work in clinics and wards	.....	None	Dr. George M. Cooper, North Carolina State Board of Health, Raleigh, N. C.
University of Pennsylvania Graduate School of Medicine	Arranged; 2-4 weeks, 75 hours	Diabetes mellitus	Individuals [1]	$150	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course in internal medicine	.....	$800 [7,9]	
MILITARY MEDICINE					
Training Division, War Department	Monthly; 170 hours	Basic Course for Officers	500 [16]	None	Training Division, Office of The Surgeon General, War Department, Washington D. C.
	Monthly; 1 month	Exemplary course	150 [16]	None	

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
MILITARY MEDICINE—Continued					
	1 month; 145 hours	Maxillo-facial and plastic surgery	12 [16]	None	
	1-3 months	Officer pool, 14 general hospitals	700 [16]	.....	
	Undetermined	Officer pool, Gulf Coast Air Corps Training Center	200 [16]	None	
	Undetermined	Officer pool, Medical Field Service School	150 [16]	None	
	1-3 months	Officer pool, Medical Replacement Training Centers	200 [16]	None	
	Undetermined	Officer pool, Medical Supply Depots and Medical Sections, General Depots	50 [16]	None	
	2 weeks; 96 hours	Photoroentgenology	20 [16]	None	
	4-6 weeks; 192 hours	Roentgenology	40-80 [16]	None	
	Monthly; 170 hours	Special course for Division Officers	$100 [16]	None	
	Continuous	Specialized Surgical Team Training	Varies [17]	None	
	251½ hours	Tropical Medicine	30 [16]	None	
Bureau of Medicine and Surgery, Navy Department	6 times a year; full time, 8 weeks	Aviation Medicine	Limited [18]	None	Bureau of Medicine and Surgery, Navy Department, Washington, D. C.
	Every 5 months; full time, 5 months	Aviation Medicine (qualifying for flight surgeon)	Limited [18]	None	
	6 times a year; full time, 8 weeks	Basic Instruction	Limited [18]	None	
	Twice a year; full time, 6 months	Deep Diving	4-12 [18]	None	
	Twice a year; full time, 6 months	Epidemiology	8-20	None	
Library of the Institute for Psychoanalysis	Oct. 5-16; MWF afternoons	Clinical discussions of war neuroses	50 [19]	None	Institute for Psychoanalysis, 43 East Ohio Street, Chicago, Illinois
Harvard University School of Medicine	To be announced; full time, 2 weeks	Military medicine and surgery	Limited [20]	None	Dr. Frank R. Ober, Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
University of Buffalo School of Medicine	To be announced	War gases	Limited [21]	To be announced	Dr. A. H. Aaron, Chairman, Department of Postgraduate and Continuation Work, University of Buffalo School of Medicine, 24 High Street, Buffalo, N. Y.
New York University College of Medicine	1 week Repeated for 6 weeks or longer	Medical aspects of chemical warfare agents		Arranged	Dr. John H. Mulholland, Assistant Dean, New York University College of Medicine, 477 First Avenue, New York, N. Y.
University of Cincinnati College of Medicine	Arranged. Full time for 3 days	Condensed course for senior gas officers	Limited [45]	Arranged	Dr. Stanley E. Dorst, Dean, University of Cincinnati College of Medicine, Eden and Bethesda Avenues, Cincinnati, O.
	Arranged. Full time for 1 week	Chemical warfare casualties	Limited [45]	Arranged	
NEUROLOGY—See Psychiatry and Neurology					
OBSTETRICS—See also Gynecology, Pathology					
The Chicago Maternity Center	September;[12] 4 months	Practical obstetrics	.....	$10	Dr. Beatrice L. Tucker, Medical Director, The Chicago Maternity Center, 1336 South Newberry Avenue, Chicago, Ill.
Harvard University Medical School	Monthly; 1 month or more	Clinical obstetrics	8 [11]	$125 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
Columbia University Faculty of Medicine	Monthly; Jan.-Oct.; full time, 3 months	Internship training	.....	$350	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
	Monthly; 1 month	Observation course	2	$100	
Duke University School of Medicine	Weekly;[22] full time, 5 days	Obstetrics and pediatrics	4-6 [38]	None [24]	Dr. G. M. Cooper, Director, Maternal and Child Health Service, North Carolina State Board of Health, Raleigh, North Carolina
OPHTHALMOLOGY—See also Radiology, Surgery					
American Academy of Ophthalmology and Otolaryngology	Oct. 12-14. Mornings	Glaucoma	Limited [43]	$6	Clare M. McGovern, Registrar, The American Academy of Ophthalmology and Otolaryngology, 58 East Washington Street, Chicago, Illinois
	Annually for 9 months starting Sept 1	Home study course	50 [23]	$10 [6]	
Columbia University Faculty of Medicine	Arranged; 15 sessions [25]	Embryology, histology and pathology of the eye	Limited [1]	$75 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
New York Eye and Ear Infirmary, School of Ophthalmology and Otology	Monthly. Part time for 1 to 3 months	General course	4-8 [9]	$40-$100 [18]	Mabel R. Stewart, Registrar, School of Ophthalmology and Otology, New York Eye and Ear Infirmary, 218 Second Avenue, New York, N. Y.

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
OPHTHALMOLOGY—See also Radiology, Surgery—Continued					
New York Polyclinic Medical School and Hospital	Monthly; 6 weeks	Refraction	6	$100	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
	Arranged; 8 weeks, 120 hours	Ocular refraction	Individuals [1]	$270	
	Arranged; 8 weeks, 96 hours	Ophthalmic histology and pathology	Individuals [1]	$200	
ORTHOPEDICS—See also Surgery					
Columbia University Faculty of Medicine	Oct. 12-Nov. 12; 10 sessions	Functional anatomy in relation to orthopedics	6-15	$40 [5,6]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Oct. 12-Nov. 6; MWF afternoons	Orthopedics in general practice	10-20	$50 [5,6]	
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
OTOLARYNGOLOGY—See also Radiology, Surgery					
Harvard University Medical School	Arranged; daily for 2 weeks	Bronchoscopy and esophagoscopy	Limited [1]	$150 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Oct.-March; full time, 6 months	Clinical laryngology	5 [1,11]	$50 [4]	
	Monthly; except April or August; full time	Clinical otology	2	$50 [4]	
	Arranged; except in April; 2 weeks	Physiology of the cochlea and vestibular apparatus	2	$50 [4]	
	Arranged	Technic of submucous resection of the nasal septum	Limited	$75 for 5 exercises [4]	
Columbia University Faculty of Medicine	When a vacancy occurs	Diagnostic procedures in otolaryngology	6 [5]	$30 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
Columbia University Faculty of Medicine	Arranged; except in July and August	Dissection of the head and neck	Minimum:	Arranged [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Arranged; 15 sessions [25]	Embryology, histology and pathology of the ear, nose and throat	Limited [1]	$75 [5]	
	Arranged; except in July and August	Surgical anatomy as applied to otology (cadaver)	2-6 [1]	Arranged [5]	
	Arranged; except in July and August	Surgical anatomy as applied to rhinology and laryngology (cadaver)	2-6 [1]	Arranged [5]	
	Arranged; Oct. 1942-April 1943; 3 weeks	Instruments and technic of bronchoscopy	.....	$250	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
New York Eye and Ear Infirmary, School of Ophthalmology and Otology	12 days. Full time or 2 days a week for 6 weeks	Broncho-esophagology	4 [8]	$250 [4,8]	Mabel R. Stewart, Registrar, School of Ophthalmology and Otology, New York Eye and Ear Infirmary, 218 Second Avenue, New York, N. Y.
	Monthly. Part time for 1 to 3 months	General course	4 [8]	$40-$100 [4,8]	
New York Polyclinic Medical School and Hospital	Monthly; 6 weeks	Clinical course	8	$100	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
Temple University Hospital	Arranged; 2 weeks	Broncho-Esophagology, gastroscopy and laryngeal surgery	12	$250	The Dean's Office, Temple University Medical School, Broad and Ontario Streets, Philadelphia, Pennsylvania
University of Pennsylvania Graduate School of Medicine	Oct. 5,1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
PATHOLOGY—See also Gynecology, Ophthalmology, Otolaryngology, Psychiatry and Neurology					
Harvard University Medical School	Monthly; except Aug.; full time	Pathology of obstetrics and gynecology [26]	2 [1]	$125 [4,27]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Aug. 10-22; 5 days a week	Pathology of tumors [26]	8 [8]	$50 [4]	
	Arranged	Research in Pathology	.....	Arranged [4,27]	
	Monthly; hours arranged	Special staining methods, autopsies [26]	4	$40 [4]	
Columbia University Faculty of Medicine	Sept. 14-Oct. 30; MWF afternoons	Gross and microscopic pathology	3-6	$50 [5,6]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
PEDIATRICS—See also Obstetrics					
Children's Memorial Hospital	Oct. 5-31; 4 weeks	Medical pediatrics, surgical specialties	.....	$100 [6]	Dr. C. A. Aldrich, Chief of Staff, The Children's Memorial Hospital, 707 Fullerton Avenue, Chicago, Illinois
Columbia University Faculty of Medicine	October;[12] 4 weeks	Clinical course	3-9	$40 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Oct. 5;[12] full time, 4 weeks	Seminar	3-12	$125 [6]	
Southern Pediatric Seminar	July 20-Aug.1	Diagnosis, prevention and treatment	.....	$25	D. Lesesne Smith, M.D., Registrar, Infants' and Children's Sanitarium, Saluda, North Carolina
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
Vanderbilt University School of Medicine	July 20-Aug. 15	Medicine and pediatrics	Limited [28]	$50 [27]	Registrar, Vanderbilt University School of Medicine, Nashville, Tennessee
PERITONEOSCOPY—See Gastroenterology					
PHYSIOLOGY—See also Psychiatry and Neurology					
Harvard University Medical School	Aug. 10-Sept. 19	General course	.....	$75 [4,27]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Arranged	Research in physiology	.....	Arranged [4]	
PHYSIOTHERAPY—See also Dermatology and Syphilology, Infantile Paralysis					
American Congress of Physical Therapy	Sept. 9-12; part or full time	21st Annual scientific and clinical session	.....	$2-15	Executive Director, American Congress of Physical Therapy, 31 North Michigan Avenue, Chicago, Illinois
Harvard University Medical School	Sept. 8; 6 months	Emergency defense course	Limited [29]	$200 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
New York Polyclinic Medical School and Hospital	Monthly 4 weeks	General course	6	$100	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
PROCTOLOGY—See also Surgery					
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
PSYCHIATRY AND NEUROLOGY—See also Military Medicine					
Harvard University Medical School	Arranged	General psychiatry or special fields	Individuals	Arranged [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Arranged	Neuro-anatomy, neurophysiology, neuropathology, clinical neurology or neurosurgery	.....	Arranged [4,30]	
	Arranged	Research in neuropathology. Elective: research on cerebrospinal fluid	.....	Arranged [4]	
Columbia University Faculty of Medicine	Oct. 5-Dec.11	Clinical, sociological and educational survey	Limited [1]	$10-$250	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
	Monthly, Oct.-May; 1 month or more	Clinical neurology	1-6	$50 per month [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Oct. 5;[31] full time, 4 weeks	Neurology and psychiatry in general practice	4-6	$100 [5,6]	
New York Academy of Medicine	Oct.12-23; full time	15th Graduate Fortnight: Disorders of the nervous system	.....	$5 [32]	Dr. Mahlon Ashford, Executive Secretary, New York Academy of Medicine, 2 East 103d Street, New York, N. Y.
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
	Arranged; 8 weeks, 240 hours	Clinical psychiatry	Individuals [1]	$160	
	Arranged; 10 weeks, 250 hours	Clinicobiologic neurology and psychiatry	Individuals [33]	$100	
PUBLIC HEALTH					
Loyola University School of Medicine	Every quarter Sept.-June	Courses in administration, laboratory, education, mental hygiene and sanitation	Individuals	Arranged	Miss McGowan, Secretary, Department of Preventive Medicine, Public Health and Bacteriology, Loyola University School of Medicine, 706 South Wolcott Avenue, Chicago, Illinois
Massachusetts Institute of Technology	July 27-Sept. 12; 6 hours a week	Health education	30	$40	Department of Public Health, Massachusetts Institute of Technology, Cambridge, Massachusetts
	Sept. 28, 1942-Feb. 6, 1943; 3 hours a week	Health education	30	$40	
	July 27-Sept. 12; 16 hours a week	Public health bacteriology	30	$85	
	Sept. 28, 1942-Feb. 6, 1943; 6 hours a week	Public health bacteriology	30	$65	

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
PUBLIC HEALTH—Continued					
	Sept. 28, 1942-Feb. 6, 1943; 8 hours a week	Public health engineering	30	$95	
	July 27-Sept. 12; 10 hours a week	Sanitation	30	$60	
Albany Medical College and New York State Department of Health	Arranged; varies [34]	Extension course	Limited [28]	$30 [36]	Extension Course Office, Albany Medical College, New Scotland Avenue, Albany, N. Y.
RADIOLOGY—See also Cardiology, Military Medicine					
Harvard University Medical School	Monthly	General roentgenology	Limited [8]	$50 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Monthly; full time	General Roentgenology: Observation of routine work	2 [8]	$100 [4]	
	Monthly	General Roentgenology: Diagnosis as interpreted from radiographic film and fluoroscopic screen	3 [11]	$100 [4]	
	October; 12 exercises	Radiological physics	.....	$10 [4]	
	Monthly; 3 days a week	Roentgenology in diseases of the eye, ear and accessory sinuses	3	$35 [4]	
Columbia University Faculty of Medicine	Sept. 28-Dec. 18; full time	Basic diagnostic roentgenology and technic	4-8 [1]	$250 [5,6,9]	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
	Sept. 28-Dec. 18; 5 days a week	Clinical roentgenology	Limited [1]	$250 [6,9]	
New York Eye and Ear Infirmary, School of Ophthalmology and Otology	Monthly. 3 mornings a week for 6 weeks	Roentgenology for ophthalmologists	2 [8]	$40 [48]	Mabel R. Stewart, Registrar, School of Ophthalmology and Otology, New York Eye and Ear Infirmary, 218 Second Avenue, New York, N. Y.
New York Polyclinic Medical School and Hospital	Monthly; except Aug.; 3 months	Advanced course in diagnostic roentgenology and radiotherapy	6 [1]	$300	Dr. F. H. Dillingham, Executive Officer, New York Polyclinic Medical School, 335 West 50th Street, New York, N. Y.
	Monthly; except Aug.; 6 weeks or 3 months	Practical roentgenological interpretation and technic	6	$150	
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
RHINOLOGY—See Otolaryngology					
SURGERY—See also Special Headings					
New Haven Hospital	Weekly starting Sept. 29. 3 days	Traumatic surgery	.....	To be announced	Dr. S. C. Harvey, New Haven Hospital, New Haven, Connecticut
Harvard University Medical School	Monthly, mornings	Clinical orthopedic surgery	1 or more	$50 [4]	Dr. Frank R. Ober, Assistant Dean, Courses for Graduates, Harvard University Medical School, 25 Shattuck Street, Boston, Massachusetts
	Monthly, except Aug.; 5 days a week	Endoscopy	2	Arranged [4]	
	October, November: [12] mornings for 1 month	Genito-Urinary surgery	4 [11]	$75 [4]	
	Monthly; mornings	Major Genito-Urinary Surgery: Clinical urology	Limited [11]	$75 [4]	
	October, November; [12] daily for 1 month	Urology	.....	$75 [4]	
Columbia University Faculty of Medicine	Arranged; 8 sessions	Blood transfusion, blood and plasma bank	1-8	$35 [5]	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
	Arranged; Sept.-June 12 sessions or more	Dissection and surgical anatomy	Minimum: 2 [1]	$125 per 12 sessions [5]	
	Oct. 5; full time, 3 months	Seminar in general surgery	4-8 [1]	$400 [5,6,9]	
	Oct. 12-23; full time	Seminar in traumatic surgery	5-30 [1]	$75 [5,6]	
	Arranged; except in July or August; 5 sessions	Surgical anatomy as applied to colon and rectal surgery (cadaver)	2 [1]	$75 [5]	
	Arranged; except in July or August; 12 sessions	Surgical anatomy as applied to thoracic surgery (cadaver)	2-6 [1]	$125 [5]	

References will be found on p. 1049

Continuation Courses for Practicing Physicians, July 25-October 25, 1942—Continued

Institution	Dates and Length of Course	Title of Course	Number of Students Accepted	Registration Fee and/or Tuition	For Detailed Information Write to
SURGERY—See also Special Headings—Continued					
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; 60 hours	Surgical technic (dog)	.....	$250 [2]	Dr. J. A. W. Hetrick, Dean, New York Medical College, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
	Arranged; 2 weeks, 85 hours	Bronchoesophagology, gastroscopy and laryngeal surgery	Individuals [1]	$250	
	Arranged; 3 weeks, 27 hours	Ophthalmic operations (cadaver)	Individuals [1]	$270	
	Arranged; 2 weeks, 20 hours	Otologic operations (cadaver)	Individuals [1]	$250	
	Arranged; 10 days, 20 hours	Rhinolaryngologic operations (cadaver)	Individuals [1]	$150	
SYPHILOLOGY—See Dermatology and Syphilology, Venereal Disease Control					
TROPICAL MEDICINE—See also Military Medicine					
Tulane University of Louisiana School of Medicine	Fall. 4½ weeks	Tropical medicine and medical parasitology [46]	Limited [8]	$300	Director, Department of Graduate Medicine, School of Medicine, Tulane University of Louisiana, 1430 Tulane Avenue, New Orleans, Louisiana
Hahnemann Medical College	Arranged		Individuals	Arranged	Dr. William A. Pearson, Dean, Hahnemann Medical College, 235 North 15th Street, Philadelphia, Pennsylvania
TUBERCULOSIS					
San Francisco Hospital	Arranged; full time, 1 week	Intensive course	Individuals	None [24]	W. F. Higby, Executive Secretary, California Tuberculosis Association, 45 Second Street, San Francisco, Calif.
City of Chicago Municipal Tuberculosis Sanitarium	Continuous; TWFS	General course	.....	None	City of Chicago Municipal Tuberculosis Sanitarium, Department of Clinics, 2049 Washington Boulevard, Chicago, Illinois
Columbia University Faculty of Medicine	Oct. 12-24; full time	General course [37]	.....	$25 [6,38]	Dean of the Faculty of Medicine, Columbia University, 630 West 168th Street, New York, N. Y.
New York Medical College, Flower and Fifth Avenue Hospitals	Arranged; daily for 1 month	Diagnosis and treatment	.....	$100	Dr. J. A. W. Hetrick, Dean, New York Medical College, Flower and Fifth Avenue Hospitals, 5th Avenue at 105th Street, New York, N. Y.
Trudeau School of Tuberculosis	Sept. 14-Oct. 9; 4 weeks	General course [39]	30	$100 [6]	Roy Dayton, Secretary, Trudeau School of Tuberculosis, Saranac Lake, N. Y.
State Tuberculosis Sanatorium	10 days or more	Diseases of the chest	Limited [23]	None [24]	Dr. J. B. McKnight, Superintendent and Medical Director, State Tuberculosis Sanatorium, Sanatorium, Texas
	10 days; throughout the year	Observation course	Limited [28]	None	
UROLOGY—See also Anatomy, Surgery					
Columbia University Faculty of Medicine	Arranged	Short courses in special subjects	Individuals [1]	Arranged	Director of the School, New York Postgraduate Medical School, 303 East 20th Street, New York, N. Y.
University of Pennsylvania Graduate School of Medicine	Oct. 5, 1942-May 29, 1943; full time, 8 months	Basic course	.....	$800 [7,9]	Dr. R. C. Buerki, Dean, Graduate School of Medicine, The Medico-Chirurgical College, 237 Medical Laboratories, Philadelphia, Pennsylvania
	Arranged; 6 weeks, 36 hours	Cystoscopy, chromoureteroscopy and pyelography	Individuals [1]	$300	
VENEREAL DISEASE CONTROL—See also Dermatology and Syphilology, Gynecology					
Medical Center, United States Public Health Service	Sept. 23-Oct. 21	General course	30	None	Austin V. Delbert, P.A. Surgeon, Medical Officer in Charge, United States Public Health Service, Hot Springs, National Park, Arkansas

1. Specialists who have had adequate preliminary training and experience.
2. If two or more students register for the course at the same time, a reduction in the fee will be made.
3. Special parts may be taken.
4. A registration fee of $5 covers all courses taken within the year.
5. Grants may be made from a scholarship fund.
6. Register-two to six weeks in advance.
7. A temporary license to practice medicine in the state is required.
8. Physicians who have had adequate preliminary training and/or are approved by the postgraduate department.
9. Arrangements may be made to take individual sections of the course at a reduced fee.
10. If taken in conjunction with the next course above/below (Gastroscopy/Peritoneoscopy), the fee for the combined course will be $125.
11. Male physicians only.
12. Repeated at intervals throughout the year.
13. Ten physicians, twenty nurses and twenty physical therapy technicians.
14. For representatives of the chapters of the National Foundation for Infantile Paralysis and others who may be qualified.
15. Preference is given to those registering for the longer course.
16. Officers in the Medical Department on active duty.
17. Officers on active duty at one of the hospitals.
18. For officers of the United States Army or Navy, or the United States Naval Reserve on active duty.
19. Interns, house officers and senior medical students who may become medical officers in the armed forces.
20. Medical Reserve Officers, United States Army.
21. Physicians attached to the Emergency War Service of Western New York.
22. Given at separate hospitals for white and Negro Physicians.
23. General practitioners licensed to practice in the state.
24. Per diem and/or maintenance provided.
25. Longer sessions arranged in units of 12 sessions each.
26. Microscope required.
27. Plus a nominal laboratory fee.
28. Holders of Commonwealth Fellowships and a limited number of other qualified physicians.
29. Course open only to those who intend to enter Government hospitals.
30. Assistantships, internships, residencies available in the fields named.
31. May be taken mornings or afternoons only at half the fee.
32. Fellows of the academy registered without fee.
33. A faculty course for staff members of mental institutions.
34. Assigned reading, monthly conferences, one week of instruction in residence.
35. Registered physicians of New York State who wish to qualify as Health Officers, Grade II.
36. Plus $10 for the required textbook.
37. Supplementary to course completed at the Trudeau School of Tuberculosis on October 9, 1942.
38. Pnysicians who have completed the course at Trudeau have already paid their fees.
39. Includes tuition for a supplementary 2-week course sponsored by Columbia University Faculty of Medicine.
40. For members of the American College of Physicians and qualified doctors seeking membership or certification in the American Board of Internal Medicine.
41. Given in New York City.
42. Given in Boston, Mass., Philadelphia, Pa., Rochester, Minn., and Minneapolis, Minn.
43. For members of the society.
44. No tuition charge to interns, residents and students.
45. Physicians selected by the National Office of Civilian Defense.
46. Venereal disease clinicians in Alabama; a few out-of-state physicians may be accepted.
47. Tuition, travelling expenses or maintenance provided by the state board of health.
48. Plus a matriculation fee of $10.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, July 18, page 969.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I.* Various centers, Sept. 14-16. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, Feb. 4. Final date for filing application is Nov. 6. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Oral. Groups A and B.* Cleveland, Jan. 14-15, 1943. Final date for filing application is Dec. 7. *Written.* Various centers, Nov. 16. Final date for filing application is Oct. 5. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 19. Final date for filing application is Sept. 1. Asst. Sec., Dr. William A. Werrell, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. *Oral. Part II.* May 1943. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups.* Chicago, Oct. 8-10. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written.* Chicago, Jan. 9-10. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written.* Richmond, Va., Nov. 9-10. Final date for filing application is Sept. 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Sept. 18. *Oral.* New York, Dec. 5-6. Final date for filing application is Aug. 1. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Final date for filing application is Oct. 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, Nov. 27-29. Final date for filing application is Sept. 30. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY. *Part I.* Oct. 7. Final date for filing application is Aug. 22. Sec., Dr. J. Stewart Rodman, 225 S Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY. February 1943 (tentative). Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

Connecticut March Report

The Connecticut Medical Examining Board reports the written examination for medical licensure held at Hartford, March 10-11, 1942. The examination covered 7 subjects and included 70 questions. An average of 75 per cent was required to pass. Thirty-seven candidates were examined, 13 of whom passed and 24 failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Northwestern University Medical School		(1941)	1
University of Maryland School of Medicine and College of Physicians and Surgeons		(1940)	1
Boston University School of Medicine		(1940)*	1
Harvard Medical School		(1940), (1941)	2
Columbia University College of Physicians and Surgeons		(1941)*	1
University of Rochester School of Medicine and Dentistry		(1939)	1
Temple University School of Medicine		(1941),* (1941)	2
University of Pennsylvania School of Medicine		(1940)	1
University of Vermont College of Medicine		(1940)	1
Université de Paris Faculté de Médecine		(1937)	1
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1938)	1

School	FAILED	Year Grad.	Number Failed
Georgetown University School of Medicine		(1941, 2)	2
University of Maryland School of Medicine and College of Physicians and Surgeons		(1941)	1
Columbia University College of Physicians and Surgeons		(1934)	1
Cornell University Medical College		(1908)	1
Syracuse University College of Medicine		(1941)	1
McGill University Faculty of Medicine		(1937)	1
Karl-Franzens-Universität Medizinische Fakultät, Graz		(1922)	1
Medizinische Fakultät der Universität Wien		(1924), (1925), (1932), (1935), (1936), (1937, 2), (1938)	8
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau		(1925)	1
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1928), (1938)	2
Regia Università degli Studi di Bologna. Facoltà di Medicina e Chirurgia		(1937)	1
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia		(1937)	1
Regia Università di Napoli Facoltà di Medicina e Chirurgia		(1937)	1
Osteopaths †			2

Nineteen physicians were successful in the oral examination for endorsement applicants held at Hartford on March 24 and May 13. The following schools were represented:

School	PASSED	Year Grad.	Endorsement of
Yale University School of Medicine		(1932),* (1936)*	N.B.M.Ex.
George Washington University School of Medicine		(1934)	N. B. M. Ex.
State University of Iowa College of Medicine		(1938)	Iowa
Johns Hopkins University School of Medicine		(1926)*	Maryland
Boston University School of Medicine		(1939)*	N.B. M.Ex.
Harvard Medical School		(1939)	N. B. M. Ex.
Tufts College Medical School		(1938)*, (1938),* (1939)*	Mass., N. B. M. Ex.
Albany Medical College		(1937)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons		(1909)*	New Hampshire, (1929),* (1937) N. B. M. Ex.
Cornell University Medical College		(1929)*	N.B.M.Ex.
Long Island College of Medicine		(1939)*	N.B.M.Ex.
University of Pittsburgh School of Medicine		(1937)	Penna.
University of Western Ontario Medical School		(1940)	N. B. M. Ex.
University of Montreal Faculty of Medicine		(1927)	Mass.

* Licenses have not been issued.

† One examined in medicine and one in surgery.

Minnesota April Report

The Minnesota State Board of Medical Examiners reports the written examination for medical licensure held at Minneapolis, April 21-23, 1942. The examination covered 12 subjects and included 60 questions. An average of 75 per cent was required to pass. Forty-seven candidates were examined, all of whom passed. Three physicians were licensed to practice medicine by reciprocity and 1 physician so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
University of California Medical School		(1941)	1
Yale University School of Medicine		(1940)	1
Northwestern University Medical School		(1941), (1941, 2)*	3
Rush Medical College		(1934), (1941)	2
Indiana University School of Medicine		(1939)	1
Tulane University of Louisiana School of Medicine		(1939, 2)	2
Johns Hopkins University School of Medicine		(1938), (1939), (1940)	3
University of Michigan Medical School		(1938)	1
University of Minnesota Medical School		(1939), (1941, 15),* (1942, 4)*	20
Washington University School of Medicine		(1940)	1
Columbia University College of Physicians and Surgeons		(1939), (1940)	2
Cornell University Medical College		(1938)	1
Ohio State University College of Medicine		(1940)	1
Temple University School of Medicine		(1940), (1941)	2
University of Pennsylvania School of Medicine		(1938), (1939), (1940)	3
Baylor University College of Medicine		(1940)	1
University of Texas Faculty of Medicine		(1939)	1
Medical College of Virginia		(1937)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Illinois College of Medicine		(1941)	Illinois
Harvard Medical School		(1939)	Wisconsin
University of Minnesota Medical School		(1940)	Virginia

School	LICENSED BY ENDORSEMENT	Year Grad.
Rush Medical College		(1926)

* These applicants received the M.B. degree and will receive the M.D. degree on completion of internship.

Colorado April Report

The Colorado State Board of Medical Examiners reports the written examination for medical licensure held at Denver, April 8-10, 1942. The examination covered 8 subjects and included 64 questions. An average of 75 per cent was required to pass. One candidate was examined and passed. The following school was represented:

School	PASSED	Year Grad.
Northwestern University Medical School		(1941)

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Accused Entitled to Bill of Particulars.—An information filed against the petitioner charged that he "did wilfully, knowingly, and unlawfully practice medicine within the State of Montana without first having obtained a certificate to practice as provided by law." The petitioner filed a motion for a bill of particulars, which was denied. He therefore applied to the Supreme Court of Montana for a writ of supervisory control directing the district court to grant an order requiring the state to furnish such bill.

The petitioner contended that the information did not sufficiently apprise him of the nature of the accusation to enable him to prepare his defense and that the refusal to grant him a bill of particulars was a violation of his constitutional rights to demand and be informed of "the nature and cause of the accusation." The respondents contended that there was no statute in Montana authorizing or giving a court a right to require the state to furnish a bill of particulars in a criminal case. The Supreme Court said, however, that it had previously recognized the existence of such a right and stated the general rule to be that when an indictment does not clearly set forth the charge against the accused he may move for a bill of particulars for specification of the acts on which the prosecution intends to rely, and such motion will be granted whenever it appears to be necessary to enable the defendant to meet the charge against him.

The respondents next contended that the information did in fact sufficiently apprise the petitioner of the charge against him. The medical practice act provides that it shall be a misdemeanor to practice medicine or surgery without a license and then states disjunctively numerous acts the doing of which constitutes the practice of medicine. The Supreme Court pointed out that the offense could thus be committed in a number of ways and said that the accused was entitled to know what the state was relying on as constituting the practice of medicine. So far as the right of the accused to a bill of particulars is concerned, the court pointed out, a prosecution under the medical practice act is analogous to one for violating the traffic regulation statute. A person can be guilty of a misdemeanor by doing any one of twenty-two different acts regarding the use of the highways and each act would be a distinct and separate offense. Certainly an accused in a prosecution under that statute would be entitled to know what particular subdivision of the statute he was accused of violating. In the opinion of the court, the petitioner in this case was entitled to a bill of particulars in order to ascertain which act or acts the state was relying on as constituting the practice of medicine, or at least which portion of the statute he was accused of violating. By pleading not guilty, the petitioner did not waive his right to a bill of particulars.

The writ of supervisory control requiring the furnishing of a bill of particulars was accordingly granted.—*State ex rel. Wong Sun v. District Court of First Judicial District in and for Lewis and Clark County, 113 P. (2d) 996 (Mont., 1941).*

Statute Authorizing Commitment of Criminal Sexual Psychopathic Persons Constitutional.—A Michigan statute (Act 165, Public Acts of 1939), which defines a criminal sexual psychopathic person as any person, not insane or feebleminded, suffering from a mental disorder coupled with criminal propensities to the commission of sex offenses, authorizes the attorney general or the appropriate prosecuting attorney, when any such person is charged with a criminal offense, to file with the clerk of the court in the same proceeding wherein the person stands charged with such criminal offense a statement in writing setting forth facts tending to show that the defendant is a criminal sexual psychopathic person. The trial court is then to appoint two qualified psychiatrists to examine the accused and to file with the court a report in writing as the results of their examination together with their conclusions and recommendations. The court subsequently is to hold a hearing to determine whether or not the accused is a criminal sexual psychopathic person and, if such a finding is made, the court is then to commit the accused to the state hospital commission to be confined in an appropriate state institution under its jurisdiction until the accused has permanently recovered from such psychopathy. The defendant, Chapman, was charged with an "act of gross indecency" but before trial on the charge the appropriate prosecuting attorney filed a petition with the court alleging that the defendant was a criminal sexual psychopathic person and the trial court appointed two psychiatrists to examine him as contemplated in the statute referred to. The psychiatrists reported in substance to the court that, while there were many suggestive signs and symptoms of schizophrenia in the defendant, they would not make a diagnosis of actual psychosis (insanity) at that time. However, they did state that the defendant had a psychosexual deviation, was homosexual and had suggestive symptoms of simple schizophrenia. They stated that his psychosexual deviation was likely to assume "a much more ominous manifestation, that of pedophilia." The trial court subsequently, after a hearing, determined that the defendant was a "criminal sexual psychopathic person" and committed him to the state hospital commission to be confined in an appropriate institution. The defendant then appealed to the Supreme Court of Michigan, questioning the constitutionality of the statute under which he was committed.

The defendant contended that the trial court was without jurisdiction to determine that he was a criminal sexual psychopathic person because the report of the psychiatrists found him to be insane and that, if he was insane, under the statute he could not be committed as a criminal sexual psychopathic person. If the defendant, said the court, had been found to be insane, he would not have been subject to commitment. The report of the psychiatrists, however, stated that, while there were many suggestive signs and symptoms of schizophrenia, a diagnosis of actual psychosis (insanity) was not made at that time and that further observation might establish the presence of that mental disorder. The report indicated long indulgence by the defendant in perverted sexual behavior, lack of inhibitions, peculiarities, flights of fancy, numerous abnormalities and symptoms of schizophrenia. While these symptoms are indicative of a psychopathic personality, they do not constitute a finding that the defendant was insane.

The court did not agree with the next contention of the defendant that the trial court was without juisdiction to commit him as a criminal sexual psychopathic person because the psychiatrists' report did not make a finding that he was not insane, which finding, he claimed, was required under the statute. The purpose of the psychiatrists' report, said the court, was to inform the trial court whether or not it was reasonable and proper to proceed with the hearing in order to determine whether or not the defendant was a criminal sexual psychopathic person. The report served that purpose. It was then for the trial court, with or without a jury, to determine whether the defendant was a criminal sexual psychopath. The trial court concluded that the evidence adduced satisfactorily established that fact. The proceedings in this case in many respects are analogous to proceedings for the commitment of a person alleged to be insane. The question of insanity is factual and the finding of the trier of facts is binding on appellate courts if there is evidence to support such a finding. That same rule of law, in the opinion of the court, applies to the instant situation, and the court concluded that the trial court had jurisdiction to conduct the proceedings and to make the order of commitment.

The defendant next contended that the statute in question denies the equal protection of the laws guaranteed by the Michigan and federal constitutions because it "limits the class of criminal sexual psychopathic persons who might be brought within its provisions only to those who are charged with a criminal offense" and that such classification makes the statute unconstitutional as class legislation. It is well recognized,

answered the court, that the legislature may make classifications of persons provided such classifications are based on substantial distinctions and are in accord with the aims sought to be achieved. Such classification, however, must be neither arbitrary nor capricious but must rest on reasonable and justifiable foundations. Was there a sound and logical basis for the legislature in enacting the act in question to restrict its operation to "criminal sexual psychopathic persons . . . charged with a criminal offense?" It is reasonable to presume that the legislature concluded that the need for such restraint as the statute imposes was greatest among that group of criminal sexual psychopathic persons apparently predisposed to transgressions against society; that is, those persons charged with other violations of the criminal law. We believe it is a reasonable and justifiable assumption that the class of sexual psychopathic persons most dangerous and most likely to commit sex crimes is that class which engages in other criminal conduct. The legislature, in the exercise of its state police power and in its efforts to afford protection, could limit the scope of a legislative act to the eradication of evil where presumably the need is greatest, even though it might constitutionally have extended the operation of its enactment to a larger class. In support of this conclusion the court quoted as follows from the opinion of the Supreme Court of the United States in *State of Minnesota ex rel. Pearson* v. *Probate Court*, 309 U. S. 270, 60 S. Ct. 523, in which a Minnesota statute providing for certain restraints for a "psychopathic personality" did not deny such a person equal protection of the laws:

> The question, however, is whether the legislature could constitutionally make a class of the group it did select. That is, whether there is any rational basis for such a selection. We see no reason for doubt upon this point. Whether the legislature could have gone farther is not the question. The class it did select is identified by the state court in terms which clearly show that the persons within that class constitute a dangerous element in the community which the legislature in its discretion could put under appropriate control. As we have often said, the legislature is free to recognize degrees of harm, and it may confine its restrictions to those classes of cases where the need is deemed to be clearest. If the law "presumably hits the evil where it is most felt, it is not to be overthrown because there are other instances to which it might have been applied."

In the present statute, continued the Supreme Court, the legislature restricted its application to that class of criminal sexual psychopathic persons who have been charged with a criminal offense, thereby restricting such act to cases where the need is deemed to be clearest and where the evil is most apparent. Such statute should not be overthrown because there may have been other instances in which it might have applied.

The court next dismissed as without any merit a contention by the defendant that the statute by a provision that at the hearing before the trial court it shall be competent to introduce evidence of the commission by such person of any number of similar crimes violated a provision of the Michigan constitution prohibiting the legislature from passing any ex post facto law. The prohibition against the enactment of an ex post facto law, the court pointed out, applies only to criminal statutes. The statute here in question is not a criminal statute nor are the proceedings under it criminal in nature but rather are analogous to civil inquests for the determination of questions of insanity.

For the reasons stated, the order of the trial court committing the defendant to the state hospital commission to be confined in an appropriate institution under the commission's jurisdiction was affirmed.—*People v. Chapman, 4 N. W. (2d) 18 (Mich., 1942).*

Malpractice: Death of Patient from Eclampsia; Alleged Abandonment.—The plaintiff engaged the defendant physician to attend his wife during childbirth. The wife died and in a subsequent suit for damages the plaintiff alleged that the death was caused by the negligent and improper treatment rendered by the defendant. From a judgment for the defendant on a directed verdict, the plaintiff appealed to the Court of Appeals of Kentucky.

The defendant was called to the plaintiff's home on the morning of Aug. 16, 1938. When he arrived there at about 7:30 a. m. he found the patient in a convulsion and was advised that she had already suffered two previously. He immediately administered a hypodermic, examined the patient's heart, took her blood pressure and said that he "found no trouble there," but believing that the patient's condition was very serious he suggested that another physician be called. Before the second physician arrived the patient had another convulsion, and magnesium sulfate was administered intramuscularly. Labor was progressing, but the two physicians agreed that more dilatation was necessary and thytuitary was administered. During the delivery the assisting physician used forceps while the defendant administered chloroform to prevent a recurrence of the convulsions. After the birth, the defendant took charge of the mother, administered pituitary to control bleeding and to regulate contraction of the uterus and remained with the patient and examined her periodically, according to his testimony, for about an hour and a half during which time the patient was unconscious. Before the defendant left he administered a heart stimulant, which he testified could not have been repeated for three or four hours, told the family where he could be reached and suggested that "if there was anything they didn't understand to call him." When he was called later he hurried back, but the patient had already died. It was agreed that the cause of death was shock and convulsions due principally to eclampsia.

The plaintiff's chief contention seemed to be that the patient's death was due to the fact that the defendant left precipitately without making suitable arrangements for the care of the patient. But, said the court, there was no evidence to indicate that the defendant precipitately left the patient. He remained at least forty-five minutes after the delivery, according to the plaintiff's own testimony. The defendant testified that he remained twice that long and that when he finally had to go to see another patient he left word as to how he could be reached. Also, the defendant testified, "Had we remained at her bedside we could not have saved her or prolonged her life; we had already done everything that medical science knew. We left nothing undone." In this he was corroborated by the physician who was called in to assist him. The expert witness called by the plaintiff admitted that in childbirth cases, where the mother has convulsions, "they die in spite of all the doctor can do." This witness also stated that the procedure adopted in delivering the baby and the question of what drugs to administer, how to administer them and with what frequency were entirely up to the attending physician in each individual case.

The Court of Appeals pointed out that a failure to effect a cure raised no presumption of want of proper care, skill or diligence on the part of a physician. No proof was found by the court to show that the death was caused by anything except shock coming at a time when the patient's condition was not such as to be able to meet it. Before the plaintiff is entitled to recover, the court said, it must be shown that the defendant was negligent and that his want of skill or neglect to do something which a physician of ordinary skill would have done resulted in death or injury. No such showing was made in this case, and the judgment for the defendant was therefore affirmed.—*Williams v. Tarter, 151 S. W. (2d) 783 (Ky., 1941).*

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., Sept. 10-12. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 10-12. Dr. Raymond B. Kepner, 547 West Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, Pittsburgh, Sept. 9-12. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

Idaho State Medical Association, Sun Valley, Sept. 16-19. Dr. F. B. Jeppesen, 105 North 8th St., Boise, Secretary.

National Medical Association, Cleveland, Aug. 17-21. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Oregon State Medical Society, Portland, Sept. 9-11. Dr. John R. Montague, 1020 S.W. Taylor St., Portland, Secretary.

Utah State Medical Association, Provo, Aug. 27-29. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Washington State Medical Association, Spokane, Aug. 17-19. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 16-18. Mr. Charles H. Crownhart, 110 East Main St., Madison, Secretary.

Wyoming State Medical Society, Cheyenne, Aug. 16-18. Dr. Marshall C. Keith, Capitol Bldg., Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Pathology, Ann Arbor, Mich.

18:363-554 (May) 1942

Studies on Leukocytosis: III. Hourly Determinations of the Maturity of Neutrophils of Normal Rabbits. G. H. Reifenstein and M. F. Hilfinger Jr., Syracuse, N. Y.—p. 363.

Id.: IV. Neutrophilic Maturity Following Intravenous Injection of Supernatant Fluid from a Sterile Exudate (Rabbit). G. H. Reifenstein, J. H. Ferguson and H. G. Weiskotten, Syracuse, N. Y.—p. 369.

*Malignant Lymphoma: Clinicopathologic Survey of 618 Cases. E. A. Gall and T. B. Mallory, Boston.—p. 381.

Fibrous Connective Tissue of the Artificially Induced Maternal Placenta in the Rat, with Particular Reference to Relationship Between Reticulum and Collagen. J. M. Wolfe and A. W. Wright, Albany, N. Y.—p. 431.

Experimental Blastomycosis in Mice. R. D. Baker, Durham, N. C.—p. 463.

Tissue Reactions in Human Blastomycosis: Analysis of Tissue from Twenty-Three Cases. R. D. Baker, Durham, N. C.—p. 479.

Pathology and Pathologic Diagnosis of Radiation Lesions in the Gastrointestinal Tract. S. Warren and N. B. Friedman, Boston.—p. 499.

Lesions Produced in the Gastrointestinal Tract by Irradiation: General Review with an Illustrative Case Report. R. M. Mulligan, Denver.—p. 515.

Synovial Sarcomesothelioma (Sarcoendothelioma). H. R. Fisher, Philadelphia.—p. 529.

Malignant Lymphoma.—Gall and Mallory point out that many generic terms have been utilized to designate diseases of the lymphatic system characterized by progressive tumor-like enlargement of lymphoid tissue with eventual fatality, and histologically by multiplication of one or more of the elements normally present in lymph nodes to the point of destruction of the nodal architecture. "Malignant lymphoma" seems to have won most general usage in this country and has the advantage of being noncommittal as to pathogenesis. In recognition of the complexity of the problem the American Association of Pathologists and Bacteriologists established a "Registry of Lymphatic Tumors" and in 1934 set the seal of the registry's approval on the schematization and terminology employed. This represented an attempted fusion of three classifications: (1) cytologic, based on morphologic recognition of component proliferating cells, (2) gross anatomic, depending on the distribution of the process throughout the organs of the body and (3) clinical, contingent on physical signs and hematologic manifestations. The authors offer a somewhat different classification, because attempts to apply the registry's terminology convinced them that it is not practical for routine use. They present a cytologic classification of malignant lymphomas and show its advantages in a clinicopathologic survey of 545 cases (73 cases of the 618 studied histologically lacked adequate clinical data). They demonstrated by multiple examinations at significant time intervals that the cytologic type is remarkably constant, although a few cases show a progressive failure of differentiation as the disease progresses. In contrast, in a classification based largely on distribution, such features as the presence or absence of leukemia, generalization versus localization and "sarcomatous" growth were considered important. These have been shown to be inconstant and changeable, thereby requiring variation in classification from time to time in order to fit the stage of the disease. The vast majority of the 618 cases from which histologic material was available could be readily divided into seven categories: stem cell lymphoma, clasmatocytic lymphoma, lymphoblastic lymphoma, lymphocytic lymphoma, Hodgkin's lymphoma, Hodgkin's sarcoma and follicular lymphoma. This differs from accepted classifications primarily in the subdivision into two types of what has generally been grouped under the heading reticulum cell sarcoma, one in which the cells are highly undifferentiated and resemble lymphoid stem cells, for which the authors have proposed the name stem cell lymphoma, and a second in which the cells show recognizable features of differentiation in the direction of tissue phagocytes, which they have termed clasmatocytic lymphoma. It has also proved useful to divide the tumors showing clear evidence of belonging to the lymphocyte series of cells into lymphoblastic and lymphocytic types depending on whether the immature or the mature cells predominate. Hodgkin's disease too has appeared divisible into lymphomatous and sarcomatous types. Follicular lymphoma has been shown to be a form of malignant lymphoma and not, as has been claimed, merely an inflammatory process. The value of this classification was put to the test of clinical correlation and, although considerable overlapping was observed, sufficiently constant differences were found in the age of onset, duration of the disease, maximal frequency or involvement of various organs and tissues, tendency to localization or generalization, the development of leukemia and the degree of radiosensitivity to delineate a series of recognizably different clinical syndromes.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

47:507-664 (April) 1942

*Pneumonoconiosis in the Talc Industry. F. W. Porro, J. R. Patton and A. A. Hobbs Jr., Ogdensburg, N. Y.—p. 507.

Calcified Tuberculoma of the Brain. L. M. Weinberger, Chicago, and F. C. Grant, Philadelphia.—p. 525.

Roentgenologic Diagnosis of Tumors of Bone. C. G. Sutherland, Rochester, Minn.—p. 534.

Atypical Giant Cell Tumor. B. L. Coley and L. E. Miller, New York.—p. 541.

Roentgenologic Aid in Differentiation of Organic from Nonorganic Mitral (Flint's) Murmurs. B. S. Epstein, Brooklyn.—p. 549.

*Cardiovascular System of American Roentgenologists Beyond the Age of Forty-Five Years. W. Raab, Burlington, Vt.—p. 555.

Significance of Psammona Calcification in Roentgen Diagnosis of Papillary Tumors of the Ovary. J. R. Lingley, Boston.—p. 563.

The Meniscus Complex in Roentgenologic Diagnosis of Ulcerating Carcinoma of the Stomach. B. R. Kirklin, Rochester, Minn.—p. 571.

Stellate Impression in the Cardiac End of the Stomach Simulating Tumor. F. M. Hodges, L. O. Snead and R. A. Berger, Richmond, Va.—p. 578.

*Diverticula of the Duodenum. L. M. Rankin, Upper Darby, Pa.—p. 584.

Platybasia, Klippel-Feil Syndrome and Sprengel's Deformity. W. Furst and H. W. Ostrum, Philadelphia.—p. 588.

Chorionepithelioma in the Male and Female as Observed Roentgenologically. J. Arendt, Chicago.—p. 591.

*Hodgkin's Disease: Five Year Survival Rate; Value of Early Surgical Treatment; Notes on Four Cases of Long Duration. D. P. Slaughter and L. F. Craver, New York.—p. 596.

Present Status of Radium Therapy. D. Quick, New York.—p. 607.

Leaded Resinous Applicator for Intraoral and Extraoral Radium Therapy. J. E. Pyott, V. F. J. Bruder, W. J. Manion and G. E. Ward, Baltimore.—p. 613.

Use of Radon Ointment as Means of Differentiation Between Radionecrosis and Recurrent Carcinoma. E. Uhlmann and A. Grossman, Chicago.—p. 620.

Pneumonoconiosis in the Talc Industry.—Porro and his co-workers attempt to correlate the dusty occupation of talc mining and milling with a definite morbidity. During the last ten years, one of the authors has noted that talc workers examined at chest clinics presented diffuse pulmonary changes believed to be at least partly due to exposure to dust. Since 1937, when the New York State compensation laws became effective, medical consultants of the New York State Department of Labor have rendered decisions that disability was produced in this industry. The authors report 15 cases in which a history of exposure to talc dust was chronologically related to the onset of symptoms. From Dreessen's analysis it appears that the dust responsible for the disabling pneumonoconiosis must be talc itself in the form of tremolite or soapstone or both, since free silica or other dust in high concentration was not found. The symptoms are those characteristic of disabling pneumonoconiosis: dyspnea, cough, chest pain and weakness. Vital capacity was extremely low. The gross pulmonary changes in all cases are stiffening of the lungs, poorly outlined grayish bands and nodules appearing in the parenchyma and moderate enlargement of the tracheobronchial lymph nodes. Emphysema is universally present but is not grossly recognized in the mild case. In all except the least involved case, extensive intrapleural adhesions are found and in all advanced cases there is a cor pulmonale. Microscopic changes consist chiefly in irregular areas and bands of cellular fibrosis surrounding the

vessels and bronchi and producing thickening of the alveolar walls. Histiocytes and fibroblasts are numerous in proportion to collagen fibers. Asbestosis bodies are frequently present in the lesions. This implies a degree of similarity between asbestosis and pneumonoconiosis due to talc. While tuberculosis or other complication may be present, pneumonoconiosis in itself is a reaction of living tissue to injury and therefore an inflammatory disease resembling other chronic inflammation. Diffuse haziness is the most constant roentgen abnormality and is probably the earliest detectable change. The general background of the pulmonary field may have a fine indefinite reticulation of lines. The appearance suggests that the haziness due to interstitial fibrosis has been modified by a fine emphysema. Another manifestation is usually general nodulation. Confluence of lesions and haziness usually begin in the areas of distribution of the lower lobe trunks. The diagnosis is made on the history of an adequate exposure and on the roentgen signs. If disability is present the characteristic symptoms are significant. If uncomplicated, the symptoms of talc pneumonoconiosis are so unlike those of pulmonary tuberculosis that a differential diagnosis is comparatively easy. In uncomplicated talc pneumonoconiosis the onset of symptoms marks the beginning of a disability from which recovery appears to be impossible. It is desirable to withdraw the worker from exposure prior to this time. There are roentgen changes before the onset of dyspnea or other subjective symptoms. The determination of vital capacity may be an effectual routine procedure in selecting workers that should be more thoroughly studied as potential subjects for withdrawal from further exposure. Standard exercise tests for the objective periodic determination of dyspnea may aid in the discovery of early pulmonary fibrosis. Measures to reduce the dust concentration should be instituted.

Cardiovascular System of American Roentgenologists.—The answers Raab obtained to a questionnaire from 344 American and Canadian roentgenologists more than 45 years of age suggest a blood pressure level slightly below the normal for all age groups. Peripheral vascular disease of a major degree and severe nephrosclerosis seemed to be relatively uncommon. The incidence of coronary disease without and with thrombosis was high. The majority of these persons were heavy smokers. Whether or not the results concerning blood pressure and peripheral vascular disease are attributable to prolonged roentgen "spray" effects on the cardiovascular system cannot be decided, but they do not seem to be incompatible with the working hypothesis that such exposure may exert a certain protective effect against an exhausting and ultimately destructive overactivity of the adrenal hormones and related substances within the myocardial and arterial muscular tissues.

Diverticula of the Duodenum.—Rankin cites a case of a diverticulum of the duodenum which presented three unusual observations: the large diverticulum was diagnosed roentgenologically before operation, it contained a gallstone, and the stone was the largest on record, about 2 inches (5 cm.) in diameter. The stone and the diverticulum were removed and the abdomen was closed. The patient made satisfactory postoperative progress for several days, but after a week her condition became retrogressive, the urinary output gradually decreased and renal dysfunction ensued in spite of treatment, the patient dying of uremia thirteen days after the operation.

Hodgkin's Disease.—From 1918 through 1935, 265 patients with Hodgkin's disease proved by biopsy were treated at the Memorial Hospital. Of the group, 26 are living, 28 have been lost to follow-up and are considered dead, and all but 1 of the others died of the disease. The study enables Slaughter and Craver to regard certain cases of Hodgkin's disease in a slightly more optimistic light than heretofore. The prognosis in a certain type of case appears more favorable than in others. This has little to do with the micropathologic picture of the disease but depends rather on anatomic location and extent. Such a case would be defined as one with only one accessible node group involved, no deep adenopathy and no systemic symptoms as evidence of hidden disease. If irradiation alone is employed in such a case, "obliterative" irradiation would be better than light palliative doses. Surgical extirpation would be justified in such a case and should be tried in the future (followed by irradiation within the limits of cutaneous tolerance) at least until enough cases are available for a revaluation of the role of surgery in the disease. The average survival period for the 265 patients from the time of beginning therapy was 33.8 months. The average survival time for the 211 who died was 24.6 months. Of the patients 17.7 per cent survived five years following treatment and 3.4 per cent more than ten years.

American Journal of Surgery, New York

56:335-522 (May) 1942. **Partial Index**

War Wounds. J. J. Moorhead, New York.—p. 338.
Fractures Sustained in War. W. Darrach, New York.—p. 341.
*Brain Injury in War. F. Kennedy, New York.—p. 343.
Outline of Treatment for Severe War Wounds of Chest. H. Neuhof, New York.—p. 346.
War Surgery of Abdominal Injuries. C. G. Heyd, New York.—p. 349.
*Potentiation of the Sulfonamides in Local Therapy of Wounds and Surgical Infections by Use of Oxidants. H. A. Goldberger, New York.—p. 353.
Pilonidal Cysts in the Army: Report of Thirty Cases Occurring in Ninety-Seven Days at Fort Sill, Okla. W. J. Pickett and A. J. Beatty, Fort Sill, Okla.—p. 375.
Acute Perforated Peptic Ulcers: Eighteen Year Survey. H. L. Berson, Brooklyn.—p. 385.
*Endometriosis (Adenomyoma) in Postoperative Scars: Analysis of Thirty-One Cases. R. G. Wyrens and L. M. Randall, Rochester, Minn.—p. 395.
Acute Perforated Peptic Ulcer Syndrome with Surgical Management: Report of 124 Surgical Cases. D. C. Donald and S. J. Barkett, Birmingham, Ala.—p. 406.
Choledocholithiasis: Clinical Study of 109 Patients Operated on. H. M. Gans, Cleveland.—p. 423.
*Acute Cholecystitis: Review of 140 Cases. S. McLanahan, H. Trout Jr., Baltimore, and W. Weary, Albany, N. Y.—p. 432.
Prevention of Shock in Spinal Anesthesia. Lillian E. Fredericks, Philadelphia.—p. 438.
Mediastinal Emphysema and Pneumothorax Following Tracheotomy for Croup. J. D. Goldberg, N. Mitchell and A. Angrist, Jamaica, N. Y.—p. 448.
Use and Abuse of Iodine in Management of Goiter. J. W. Hendrick, Amarillo, Texas.—p. 455.
Burns and Scalds: Their Etiology and Prognosis. J. M. Hoffman, Chicago.—p. 463.
Sulfallantoin in Treatment of Wounds. A. E. Imler, Philadelphia.—p. 469.
Retroperitoneal Hemorrhage, with Special Reference to Accompanying Paralytic Ileus. J. E. Karabin, Evanston, Ill.—p. 471.

Brain Injury in War.—Kennedy presents a routine procedure for the treatment of cerebral injuries of war. Denny-Brown has demonstrated experimentally that a head injury to produce unconsciousness must accelerate the movement of the brain to not less than 28 feet per second. Such acceleration usually does not occur if the skull is penetrated by a metal fragment traveling at a high speed. Therefore a man injured in this manner becomes unconscious immediately, and usually he has not been made unconscious by the impact of the missile but by the missile having ploughed through such extensive area of cerebral tissue as to make recovery extremely unlikely. On the other hand, a nonpenetrating blow on the head will often cause immediate unconsciousness without necessarily having destroyed or even permanently injured any cerebral area. Today, because of the sulfonamide derivatives, if cerebral injuries are treated early it is possible to prevent their infection. The procedure presented is as follows: The hair is clipped, the scalp washed with soap and water and local anesthesia induced. Morphine should not be used. Large bleeding vessels are caught with hemostats or by rubber tubing placed around the forehead. Wounds should be filled with sulfanilamide or sulfapyridine; débridement should be as thorough as possible. Antitetanic serum should be given. Treatment for shock is to be instituted immediately and operation delayed for twenty-four to thirty-six hours, so that patients can be sent back to a place where facilities for roentgen study are available. Such a "head station" should be as near the front area as is militarily possible. It is now possible to treat such patients with a closed operation. The blood clot in the track of the missile is sucked out and irrigated with warm saline solution. A rubber catheter is best for exploration. Any wound big enough to be explored with the finger is hardly worth exploring. The track should be filled with sulfanilamide powder before it is closed. The attempt to remove inaccessible bone or metal fragments may do more harm than was done by the enemy who put them in. After this procedure, sulfonamide drugs should be continued. Pentobarbital therapy should be started at once and continued for a year or more. If the wound has not been treated within forty-eight

hours it must be treated as an infected open wound. Increased pressure and acute cerebral edema are dealt with by dehydration. In the care of nonpenetrating head injuries shock is treated by intravenous injection of 100 cc. of a 50 per cent solution of hypertonic dextrose or blood serum. Lumbar puncture should be performed for diagnosis and treatment and the hypertonic dextrose solution repeated to reduce increased intracranial pressure. Caffeine with sodium benzoate, rectal taps, elevation of the head of the bed, operative procedures for suspected meningeal hemorrhage, antimeningococcus serum in suitable cases, antitetanus serum for all patients with a scratch, right subtemporal decompression for comatose patients who do not respond to the foregoing procedures within three days and elevation of uncomplicated depressed fractures of the skull are employed after the acute stage of shock has passed. Surgical intervention for this group of patients may often be safely postponed for many days.

Potentiation of Sulfonamide Derivatives by Oxidants in Local Therapy of Wounds.—Goldberger states that his experience in 884 cases leads him to believe that the most effective local antibacterial agent is represented by a combination of sulfanilamide and sulfathiazole with an oxidant. Depending on the nature of the wound or infection, a choice of powder, ointment, paste, jelly, solution or impregnated gauze can be used. The activating agent varies with the vehicle: for the powder form zinc peroxide is favored, for the ointment and the paste azochloramide and zinc peroxide, and for solutions iodine, azochloramide and potassium permanganate. Regardless of the form of the medication used, a local excess of sulfonamides must be made constantly available for absorption by the tissues and to make up for that lost through excretion. The addition of a wetting agent, such as sodium tetradecyl sulfate, will enhance the effectiveness of the suspensions and ointments. The combination of a sulfonamide, an oxidizing agent and a wetting agent comprises the most effective local antibiotic mechanism. The combination of sulfanilamide and sulfathiazole is more effective than either alone. Idiosyncrasy to local therapy is rare. Potentiated sulfonamides are also antibacterial and antibiotic to other unicellular organisms: amebas, paramecia, trichomonads, spermatozoa and certain fungi. Clinical and laboratory studies indicate that their action depends on a direct attack on the bacterial cells by oxidation, thus approximating the ideal surgical antiseptic, which is harsh to bacteria and kind to tissues.

Endometriosis in Scars.—Wyrens and Randall collected 31 cases of true endometriosis in postoperative scars from the 1916 to 1941 records of the Mayo Clinic. The endometriosis was proved by microscopic study of the specimens; in 15 it followed uterine suspension operations, in 4 cesarean section, in 4 salpingectomy, in 2 hysterectomy, in 2 myomectomy, in 1 simple appendectomy, in 1 drainage of an appendical abscess, in 1 inguinal herniorrhaphy and in 1 some type of pelvic operation performed elsewhere. In most of the cases the lesion followed operations performed on the uterus or fallopian tubes, but in the performance of most of them the lining of these organs was not exposed. A few of the tumors seem to have originated from exposed portions of endometrium and to have invaded the abdominal wall secondarily, but others were separated from the uterine lining. The best evidence for the etiology of this condition, which is unknown, points toward transplantation or invasion (migration) of endometrium from the lining of the uterus. The endometriomas in question resemble endometrium, microscopically, and in 1 an unabsorbed suture was presented, which may or may not represent the contaminating vehicle during the original operation. In many cases in which the condition followed ventral suspension of the uterus the round ligaments were involved in endometriosis at the points at which they were sutured to the anterior abdominal wall. Pain, worse at the menstrual period, and a palpable nodule, were the most common complaints. Few of the tumors discharged a bloody fluid at the menstrual period. In a few cases there were no symptoms. The differential diagnosis includes keloids, desmoids, fibromas, neuromas, incarcerated omental hernias and uterine or tubal fistulas. If the condition is uncomplicated, cure may be obtained by wide excision. One recurrence was encountered, undoubtedly caused by inadequate excision at the first operation.

Acute Cholecystitis.—McLanahan and his associates review the records of 140 patients with acute cholecystitis who were operated on by twenty-seven operators at the Union Memorial Hospital between September 1923 and November 1940. Sixty-three per cent of the patients were between 30 and 60 years of age, 34 were more than 60. Nausea or vomiting or both occurred in 85 per cent. Pain was almost a universal symptom. Jaundice was present in 20 per cent of the 96 with definite records. There were twelve deaths; seven occurred among the 28 undergoing drainage of the gallbladder and five among the 112 undergoing cholecystectomy. The gallbladders of the 7 patients who died following cholecystostomy were gangrenous; five of them had perforated. Of the 5 dying after cholecystectomy, the gallbladders of 3 were gangrenous and those of 2 were acutely inflamed without gangrene. Approximately half of the patients had had symptoms for more than a week. The mortality (three deaths) was highest among the 14 patients operated on in the first twenty-four hours; it became high again only after a week. Some postoperative complication developed in 31 per cent of the patients. The complications were pulmonary, myocardial, peritoneal, hemorrhagic or vascular.

Annals of Surgery, Philadelphia

115:721-880 (May) 1942

*Intestinal Obstruction from Gallstones. H. L. Foss and J. D. Summers, Danville, Pa.—p. 721.
Surgical Aspect of Congenital Absence of the Gallbladder: Report of Two Cases. G. G. Finney and J. K. Owen, Baltimore.—p. 736.
Anatomy of the Attachments of the Diaphragm: Their Relation to Problems of Surgery of Diaphragmatic Hernia. J. D. Rives and D. D. Baker, New Orleans.—p. 745.
Operation for Cure of Inguinal Hernia. E. V. Mastin, St. Louis.—p. 756.
Method for Disposal of the Sac in Operations for Oblique Inguinal Hernia. J. D. Collins, Portsmouth, Va.—p. 761.
Use of the Cutis Graft in Repair of Certain Types of Incisional Hernias and Other Conditions. J. E. Cannaday, Charleston, W. Va.—p. 775.
Retrovaginal Hernia. W. C. Dixon, Nashville, Tenn.—p. 782.
*Acute Hematogenous Osteomyelitis. H. Mahorner, New Orleans, and A. P. Crain Jr., Shreveport, La.—p. 790.
Splenectomy. A. O. Singleton, Galveston, Texas.—p. 816.
*Use of Estrogenic Substances in Preoperative and Postoperative Treatment of Hyperthyroidism: Further Observations. A. H. Storck and J. Sabatier, New Orleans.—p. 821.
Intestinal Antisepsis with Sulfonamides. W. M. Firor, Baltimore.—p. 829.
Ureteral Transplantation and Cystectomy: Comparison of Results After Eight Years. A. G. Brenizer, Charlotte, N. C.—p. 833.
*Treatment of Trichomonas Vaginalis Vaginitis with Lactobacillus. L. Brady and R. D. Reid, Baltimore.—p. 840.
*Acoustic Tumors, with Special Reference to End Results and Sparing of the Facial Nerve. A. Nielsen, New Haven, Conn.—p. 849.
Abducens Nerve (VI) Paralysis Following Spinal Anesthesia. I. R. Hayman and P. M. Wood, New York.—p. 864.
Deformed Chin and Lower Jaw. S. L. Scher, New York.—p. 869.
An Improved Biopsy Punch. M. L. Weinstein, M. Schindler and E. L. Adams, Chicago.—p. 880.

Intestinal Obstruction from Gallstones.—Foss and Summers report 10 personally observed cases and review 140 most significant records of the past two decades of similar cases. The relative incidence of intestinal obstruction from gallstones varied from 1 to 5 per cent. There were 130 women and 20 men, a ratio of 6.5:1; this corresponds to the relative incidence of cholelithiasis in the two sexes. The majority of patients were in the sixth and seventh decades of life. A gallstone large enough to cause intestinal obstruction rarely passes by way of the common duct, the most common route being a fistula between the fundus of the gallbladder and some portion of the duodenum. The sequence of events usually is cholelithiasis, ulceration and erosion of the gallbladder wall, pericholecystitis and the formation of a fistulous tract. Twenty-three of the 150 patients had no history suggestive of disease of the gallbladder, and 48 gave a history of epigastric pain interpreted as being associated with the process of perforation. A stone that enters the small intestine may pass spontaneously, but more often it produces characteristic intermittent symptoms of obstruction. The most frequent site for the stone to lodge is in the terminal portion of the ileum. Only early surgical intervention will lower the high mortality rate. The finding of a faceted stone at operation may be indicative of possible multiple stones.

Acute Hematogenous Osteomyelitis. — Mahorner and Crain compare a series of 66 cases of primary acute hematogenous osteomyelitis admitted to Charity Hospital between 1937 and 1940 with a series of 112 cases admitted between 1930 and 1936. In the 66 the mortality was 6.6 per cent as contrasted with 24 per cent for the 112 cases. The important features responsible for the higher mortality were unjustified emergency operations without proper preoperative preparation, failure to reestablish preoperatively a normal physiologic state by fluid and electrolyte replacement and blood transfusions. New chemotherapeutic measures and immunotherapy have undoubtedly had a favorable influence. The study showed that operation performed after preparation is not a deleterious factor in itself and that opening the bone after preparation is no more harmful than incision and drainage. Evacuation of pus by simple incision or osteotomy would seem to be a favorable therapeutic measure. Osteotomy apparently does not influence the extent of osseous involvement. A measure of extreme importance from the operative point of view is vein ligation for patients with a persistent positive blood culture. Immobilization in a plaster encasement deserves wider application.

Estrogenic Substances in Hyperthyroidism.—Storck and Sabatier report 11 cases of hyperthyroidism treated preoperatively with estrogens. The average basal metabolic rate for the group was + 47.7 per cent; 4 of these were iodine fast and 4 manifested such toxicity as to be considered to require multiple stage operations. The response to preoperative treatment and operation of this group is compared with corresponding observations made in 11 cases of hyperthyroidism in which estrogenic therapy was not employed. The patients who received estrogen therapy looked and felt better than did the control group. This difference was most pronounced during the immediate postoperative period. An average preoperative lowering of pulse rate equal to that which occurred in the control group was observed in the estrogen treated patients even though more of them were iodine fast at the time of admission. The average peak pulse rate of the first postoperative day in the cases in which estrogen was administered was lower than the average peak pulse rate on the same day in the control group. No crisis occurred in the estrogen group. Estrogen therapy may be of value both in the prevention and in the treatment of thyroid crisis, especially following a first stage lobectomy. Small doses of estrogenic substances are as effective as large doses, if not more so. Estrogen therapy is most effective when administered for from four to seven days preceding the operation when subtotal thyroidectomy is performed. It seems advisable to continue estrogen therapy for several days following the first stage and to reinstitute estrogen therapy preceding the second stage, especially if there is a lapse of more than a week between operations. Estrogen therapy is valuable only as an adjunct in the surgical treatment of hyperthyroidism. No significant difference has been observed in the response to estrogen by patients with toxic diffuse goiter and those with toxic nodular goiter. The number of cases in which estrogen therapy has been employed is too small to be statistically significant.

Treatment of Trichomonas Vaginalis Vaginitis with Lactobacillus.—Brady and Reid treated vaginitis due to Trichomonas by introducing viable lactic acid forming bacilli into the vagina. Sterile skim milk is inoculated with a culture of Lactobacillus bulgaricus. After forty-eight hours' incubation, 1,000 cc. of this culture is mixed with 325 Gm. each of XXXX sugar and milk sugar. This is thoroughly dissolved in the milk, and the mixture is spread in layers on enamel pans and dried in a vacuum oven at 37 C. The mixture is scraped from the pans, broken into bits and replaced in a drier to complete desiccation. When completely dried, 6 cc. of white liquid petrolatum and 38 Gm. of starch are added. The mixture is then pressed into tablets. The finished tablets weigh 1.3 Gm. and represent 1.25 cc. of original culture. A bivalve speculum is introduced, the vagina is dried with cotton and two lactobacillus tablets are inserted high in the posterior fornix. The vaginal orifice is then plugged with a tampon of nonabsorbent cotton. The next day the tampon is removed, material is taken from the vagina for microscopic study and the treatment is repeated daily for from four to six days. The patient is then told to insert one lactobacillus tablet high in the vagina each night and to take douches only if she becomes uncomfortable from unabsorbed particles coming out of the vagina and causing irritation. A white vinegar douche (5 per cent acetic acid) is recommended in a strength of from 2 to 4 tablespoons to 2 quarts of water. Two douches a week are sufficient. This home treatment is continued from three to six weeks and longer if necessary. If the organisms promptly disappear, the tablets need be used only every other night. It is especially important that they be used while the patient is menstruating, as that is the time when the vaginal defenses against the trichomonads are weakest. In a series of 50 patients thus treated all showed immediate improvement and in many instances the organisms disappeared at once. Nevertheless treatment was continued from three to six weeks and, when necessary, longer. Six patients who had been thought cured had recurrences; perhaps in some instances these were reinfections. The recurrence cleared up more rapidly than did the first infection. Forty-eight of the series now have negative smears and are asymptomatic. Many of these patients have now been followed for six months.

Acoustic Tumors.—Nielsen analyzes the late results of Olivecrona's series of acoustic tumors. In this series of 130 patients with surgically verified acoustic neurinoma the youngest patient was 18 years of age and the oldest 68. The acoustic nerve was involved in 99.2 per cent, nystagmus was present in 96.2 per cent, choked disks were found in 90.8 per cent and roentgenograms were positive in 81.5 per cent, as evidenced by changes at the internal acoustic meatus. Improved operative technic has lowered the mortality rate to 11.1 per cent in the group of complete extirpations during 1937 to 1939. Complete removal of the tumor is the operation of choice because recurrences are rare, the danger of secondary hemorrhage is much less than in incomplete removal and the presence of scar tissue in secondary operations increases the danger and makes saving of the facial nerve almost impossible. Radical removal should be attempted in all cases except those in which the tumor is cystic or the saving of the facial nerve imperative. If the saving of the facial nerve is imperative an almost complete extirpation may still be possible by leaving a bridge of tumor tissue covering the facial nerve from the internal acoustic porus to the pons. The facial nerve may be saved in practically all cases of intracapsular enucleation. In the group of subtotal extirpation, improved technic has made saving of the facial nerve possible in the majority of instances. When complete extirpation was performed the facial nerve was spared in 15, or 65 per cent, of 23 cases. The morbidity as expressed in inability to work has been lowered to 12.4 per cent in the group of complete extirpations. Of the 103 survivors followed up, 78, or 75.7 per cent, had full or diminished earning power, exclusive of the convalescent patients.

Archives of Ophthalmology, Chicago

27:845-1046 (May) 1942

Relation of Field Contraction to Blood Pressure in Chronic Primary Glaucoma. A. B. Reese and J. S. McGavic, New York.—p. 845.
Obstacle to Squint Training—Amblyopia. J. B. Feldman and Annabel F. Taylor, Philadelphia.—p. 851.
Treatment of Pneumococcic Corneal Lesions. W. P. Chamberlain Jr., Cleveland.—p. 869.
Review of Color Vision, with Some Practical Suggestions for Medical Examiners. A. H. Schwichtenberg, Randolph Field, Texas.—p. 887.
Inclusion of Sclera in Corneal Transplantation: Gross and Microscopic Study. R. Castroviejo and A. J. Elliot, New York.—p. 899.
Operation for Removal of Pterygium. F. W. Stocker, Durham, N. C. —p. 925.
Abscess-Forming Follicular Conjunctivitis. R. Waldapfel, Grand Junction, Colo.—p. 929.
Primary Orbital Melanoma: Case Report with Review of Literature. A. Rottino and A. S. Kelly, New York.—p. 934.
Mechanism of Accommodation. M. P. Koke, San Diego, Calif.—p. 950.
Pupillographic Studies: I. Present State of Pupillography; Its Method and Diagnostic Significance. O. Löwenstein and E. D. Friedman, New York.—p. 969.
Resection of Levator Palpebrae Muscle by the Conjunctival Route for Ptosis: Simplified Technic. S. A. Agatston, New York.—p. 994.
Penetration of Sulfathiazole into the Eye: Further Studies. H. G. Scheie and I. H. Leopold, Philadelphia.—p. 997.
Duplex Rod with Handle for Routine Investigation of Extraocular Muscles. P. Montalvan, New York.—p. 1005.

Archives of Pathology, Chicago

33:573-734 (May) 1942

Normal and Pathologic Proliferation in the Breast, with Special Reference to Cystic Disease. Helen Ingleby, Philadelphia.—p. 573.

Pathologic Changes Following Injections of Ferrihemate (Hematin) in Dogs. W. A. D. Anderson, St. Louis; D. B. Morrison and E. F. Williams Jr., Memphis, Tenn.—p. 589.

Composition of the Liver: Its Uniformity with Respect to the Concentration of Certain Biochemical Constituents in Different Parts of the Same Liver. G. M. Rourke and J. D. Stewart, Boston.—p. 603.

Sclerotic Areas in Skulls Affected with Paget's Disease. B. Orban, Chicago.—p. 607.

Use of Serum Ultrafiltrate in Tissue Cultures for Studying Deposition of Fat and for Propagation of Viruses. H. S. Simms and M. Sanders, New York.—p. 619.

Experimental Peptic Ulcerations by Vasomotor Episodes (Pitressin Episodes) and Autonomic Disturbances. M. Berg, Chicago.—p. 636.

Fatty Changes in the Liver from Different Causes: Comparative Studies of the Lipid Partition. S. J. Thannhauser and H. Reinstein, Boston.—p. 646.

Occurrence of Atheroma in the Aorta in Rabbits with Renal Hypertension. L. V. Dill and C. E. Isenhour, New York.—p. 655.

Spontaneous Solitary and Multiple Mast Cell Tumors ("Mastocytoma") in Dogs. F. Bloom, Flushing, N. Y.—p. 661.

Role of Parasite Pigment (Ferrihemic Acid) in Production of Lesions in Malaria. W. A. D. Anderson, St. Louis, and D. B. Morrison, Memphis, Tenn.—p. 677.

Synovialoma: Case Report. P. Gross and D. W. Cameron, Pittsburgh.—p. 687.

Syphilitic Aneurysm of the Superior Mesenteric Artery: Case Report. C. H. Binford, Detroit.—p. 691.

Simultaneous Soap-Wax Dehydration and Infiltration of the Human Heart: Method for Permanent Preservation. R. J. Lebowich, F. A. Opps and L. Procita, Gloversville, N. Y.—p. 696.

Dissecting Aneurysm of the Aorta. S. Sailer, Cincinnati.—p. 704.

Bulletin of Johns Hopkins Hospital, Baltimore

70:335-398 (April) 1942

Electroencephalogram in Addison's Disease. W. C. Hoffman, R. A. Lewis and G. W. Thorn, Baltimore.—p. 335.

Relation Between the Chemical Structure of Fats and Their Ability to Produce Gastric Inhibition. H. C. Tidwell, Dallas, Texas, and Eugenia S. Cameron, Baltimore.—p. 362.

Isolation and Identification of the Gonococcus. R. D. Reid, Baltimore.—p. 370.

*Oral Treatment of Hay Fever with Ragweed Pollen. Elizabeth H. Iliff and L. N. Gay, Baltimore.—p. 378.

Further Observations on Treatment of Intractable Bronchial Asthma by Bilateral Resection of Pulmonary Plexus. L. N. Gay and W. M. Rienhoff, Baltimore.—p. 386.

Oral Treatment of Hay Fever.—Iliff and Gay observed 62 patients with hay fever who took ragweed pollen orally before the season started and 20 during the season. The beginning dose was 500 Noon units. This was increased according to a definite schedule until daily totals varying from 60,000 (at the sixteenth dose) to 240,000 units were reached. In preseasonal treatment the dose was given soon after a meal two or three times a week and increased to daily intake with the onset of symptoms. In coseasonal treatment it was given daily or, in a few cases, three times a day until the maximal dose was reached. Of the patients treated preseasonally 3 obtained almost complete relief, 10 good relief, 25 fair results, 21 were not benefited and 3 stopped treatment because of reactions. Of the 20 treated coseasonally 14 were mildly benefited, 4 obtained no relief and 2 stopped treatment. For comparison, of 37 patients treated perennially or preseasonally by hypodermic administration during the same season 13 had excellent, 11 good, 9 fair results, and 4 failed to obtain any benefit. An analysis of the factors involved in the 25 who failed to obtain benefit from oral treatment revealed that 1 had pansinusitis during the season, 11 gave definite evidence of other allergy or of psychogenic factors, 2 were treated coseasonally too late, 3 had received previous injection treatment without benefit and in 8 there were no contributory factors. Studies of the reagin content of the serum of 7 patients failed to show any change. Reactions in 33 patients were for the most part not severe and were fairly readily controlled. Almost all were gastrointestinal.

Connecticut State Medical Journal, Hartford

6:317-404 (May) 1942

Faith versus Fear. C. C. Burlingame, Hartford.—p. 324.

Anesthesia and Analgesia in Obstetrics: With Report on Use of Evipal Soluble. H. Thoms and H. C. Taylor, New Haven.—p. 327.

Physiotherapy in Fractures. E. D. O'Donnell, New Haven.—p. 332.

From Consumption to Tuberculosis in Connecticut. D. R. Lyman, Wallingford.—p. 335.

Journal of Experimental Medicine, New York

75:465-566 (May) 1942

Localized Action on the Spinal Cord of Intramuscularly Injected Tetanus Toxin. G. H. Acheson, E. D. Ratnoff and E. B. Schoenbach, Boston.—p. 465.

Copper and Cobalt: Related Hemoglobin Production in Experimental Anemia. Freida S. Robscheit-Robbins and G. H. Whipple, Rochester, N. Y.—p. 481.

Red Cell and Plasma Radioactive Copper in Normal and Anemic Dogs. H. Yoshikawa, P. F. Hahn and W. F. Bale, Rochester, N. Y.—p. 489.

*Antibody Response of Human Beings Following Vaccination with Influenza Viruses. G. K. Hirst, E. R. Rickard, L. Whitman and F. L. Horsfall Jr., New York.—p. 495.

Arterial Hypertension in Rats: I. Methods. H. A. Schroeder, New York.—p. 513.

Id.: II. Effects on the Kidneys. H. A. Schroeder and C. Neumann, New York.—p. 527.

Toxemia of Pregnancy in the Guinea Pig. E. J. Foley, Notre Dame, Ind.—p. 539.

The Hypophysis and Secretion of Insulin. B. A. Houssay, V. G. Foglia, F. S. Smyth, C. T. Rietti and A. B. Houssay, Buenos Aires, Argentina.—p. 547.

Antibody Response to Influenza Vaccination.—Hirst and his collaborators used eleven different preparations of influenza virus to vaccinate approximately 150 human beings with each one. The antibody response to these vaccines was measured by the in vitro agglutination inhibition test. The comparison of the geometric mean titers of serums taken two weeks after vaccination showed that: 1. There was a wide individual variation in the antibody response of human beings to the same preparation of influenza virus administered subcutaneously. The amount of antibody produced by a group with a low prevaccination antibody level was nearly the same as that produced by groups with higher initial levels. 2. The use of the X strain of distemper virus in the influenza vaccine did not enhance the antigenicity of the influenza virus present. 3. Within certain limits the mean antibody response increased according to the amount of virus injected. When the amount injected was large, the magnitude of the antibody response was the same as that which follows actual infection. 4. When the vaccine was prepared from allantoic fluid there was no significant difference in the antibody response to active virus, formaldehyde inactivated virus, heat inactivated virus or virus inactivated by the drying process. 5. Ground infected chick embryos, when diluted with infected allantoic fluid, gave a greater antibody response than allantoic fluid alone (when the virus remained active). The antigenicity of such a preparation was diminished when the virus was inactivated by formaldehyde. 6. The antibody level six and nine weeks after vaccination dropped from the two week postvaccination level. In a small group the level at five months was still further reduced. Individuals who had higher titers tended to lose the antibodies faster than did those who had lower levels.

Journal of Nat. Cancer Inst., Washington, D. C.

2:403-530 (April) 1942

Penetration of Ultraviolet Radiation into Skin as Factor in Carcinogenesis. J. S. Kirby-Smith, H. F. Blum and H. G. Grady.—p. 403.

Methods for Separation of Epidermis from Dermis and Some Physiologic and Chemical Properties of Isolated Epidermis. J. P. Baumberger, V. Suntzeff and E. V. Cowdry.—p. 413.

Effect of Certain Sulfur-Containing Compounds on the Initiation of Mitosis in Ameba Proteus. H. W. Chalkley.—p. 425.

Effect of Low Cystine Diet on Growth of Various Strains of Mice. Florence R. White and J. White.—p. 449.

Extraction and Ultracentrifugation of Mammary Tumor Inciter of Mice. W. R. Bryan, H. Kahler, M. B. Shimkin and H. B. Andervont.—p. 451.

Apparatus for Milking Mice. H. Kahler.—p. 457.

Production of Gastric Lesions in Rats by Fasting, Partial Inanition and Deficiency of Certain Dietary Constituents. H. P. Morris and S. W. Lippincott.—p. 459.

Transplantable Malignant Hemangioendothelioma of the Liver in the Mouse. J. E. Edwards, H. B. Andervont and A. J. Dalton.—p. 479.

Disappearance of Intravenously Injected Methylcholanthrene in Mice of Different Susceptibility to Pulmonary Tumors. E. Lorenz and M. B. Shimkin.—p. 491.

Factors Influencing the Induction of Pulmonary Tumors in Strain A Mice by Carcinogenic Hydrocarbons. M. B. Shimkin and E. Lorenz.—p. 499.

Distribution of Acid and Alkaline Phosphatase in Tumors, Normal Tissues and the Tissues of Tumor-Bearing Rats and Mice. J. P. Greenstein.—p. 511.

Titration of Liver Catalase Activity of Normal and of Tumor-Bearing Rats and Mice J. P. Greenstein.—p. 525.

Journal of Neurophysiology, Springfield, Ill.

5:169-244 (May) 1942

Impedance Changes in Frog's Muscle Associated with Electrotonic and "Endplate" Potentials. B. Katz, Sydney, Australia.—p. 169.
Some Physiologic Aspects of Audiogenic Seizures in Rats. D. B. Lindsley, F. W. Finger and C. E. Henry, Providence, R. I.—p. 185.
Responses During Refractory Period at Myoneural Junction in Isolated Nerve-Muscle Fiber Preparation. S. W. Kuffler, Sydney, Australia.—p. 199.
Effect of Eserine on Neuromuscular Transmission. J. C. Eccles, B. Katz and S. W. Kuffler, Sydney, Australia.—p. 211.
Excitability of Cerebral Cortex in Infant Macaca Mulatta. Margaret A. Kennard and W. S. McCulloch, New Haven, Conn.—p. 231.
Effects of Presynaptic Volleys on Spread of Impulses over the Soma of the Motoneuron. B. Renshaw, New York.—p. 235.

Kentucky Medical Journal, Bowling Green

40:159-200 (May) 1942

Treatment of Anemia. M. F. Beard, Louisville.—p. 161.
What Progress Has Been Made in Cancer? L. W. Frank, Louisville.—p. 165.
Peritoneoscopy: An Additional Diagnostic Method. J. A. Vesper Jr., Newport.—p. 169.
Sinusitis and Its Relation to General Systemic Disease. A. L. Bass, Louisville.—p. 172.
Some Observations by the Army Doctor on Physical and Mental Defects Found in the Selective Service Men Sent for Duty at Fort Knox. C. D. Holmes, Fort Knox.—p. 176.
Experiences of a State Medical Officer. W. N. Lipscomb, Louisville.—p. 180.
Experience and Impressions of a Rural Examining Physician. E. S. Dunham, Edmonton.—p. 181.
Draft Board Examinations in 1917 to 1918 and in 1940 to 1941. J. C. Graham, Greensburg.—p. 183.
Management of Acute Middle Ear Infection. A. L. Juers, Louisville.—p. 190.

Medical Annals of District of Columbia, Washington

11:125-166 (April) 1942

From Civilian Practice to Military Service. D. L. Borden, Washington.—p. 125.
Diseases of the Pancreas: I. Acute Diseases. R. J. Coffey, Washington.—p. 131.
*Histamine in Treatment of Raynaud's Disease and Acrocyanosis. I. Shulman, Washington.—p. 137.
Management of Psychoneuroses. I. Rodis, Washington.—p. 143.
Intramyocardial Bullet Localized by Roentgenkymography: Report of Case. M. Silverman, Washington, and A. M. Cove, Brooklyn.—p. 146.

Histamine in Raynaud's Disease and Acrocyanosis.—Histamine by iontophoresis was employed by Shulman in the treatment of 10 patients with Raynaud's disease and in 2 with acrocyanosis limited to the upper extremity. The average blood flow before iontophoresis as measured by the Hewlett plethysmograph was 7.97 cc. Following treatment there was an average increase in 11 of the 12 patients of 3.51 cc., or 44 per cent. The extremes were 1.10 and 8.71 cc. One patient showed no change. The hand capacity volume following iontophoresis increased to an average of 12.18 cc. as compared to an average of 8.26 cc. during the resting state before treatment. The patient who had no change in rate showed a decrease of 2.2 cc. in capacity volume. Symptomatically the patients have been afforded much relief, and the frequency and duration of the attacks (in Raynaud's disease) was decreased.

Missouri State Medical Assn. Journal, St. Louis

39:131-158 (May) 1942

*Intraspinal Protrusion of Intervertebral Disks: Observations on Diagnosis. R. M. Klemme, W. Scott and R. D. Woolsey, St. Louis.—p. 131.
Strangulated Hernia: Successful Reduction and Repair After Thirteen Days: Case Report. H. F. Burkwall, St. Joseph.—p. 132.
Diverticula of Duodenum. J. H. Hershey, St. Louis.—p. 134.
Volvulus of Stomach: Report of Case. C. A. W. Zimmermann, Cape Girardeau.—p. 139.
Fifty Years Ago: Surgery at the Time the St. Louis Surgical Society Was Founded. R. E. Schlueter, St. Louis.—p. 141.

Intraspinal Protrusion of Intervertebral Disks.—Klemme and his associates believe that a positive diagnosis of protruded intervertebral disk can be made only when definite fluoroscopic evidence is obtained by the intraspinal use of iodized oil. The iodized oil can be injected and then removed at the conclusion of the fluoroscopy. They describe a special type of needle which facilitates the procedure. The needle has a second opening on the back just above the bevel. This allows a free flow of fluid when the usual opening may be closed by a nerve root or arachnoid. The most important single feature of the entire procedure is to introduce the needle in the exact midline. Its position is checked fluoroscopically, and if it is not in the midline it is reintroduced. The iodized oil must be maneuvered into every part of the spinal subarachnoid space that is to be investigated. The filling defect must be constant on repeated examinations and must persist with the patient in different positions. The iodized oil must be kept together in one single mass as it is followed past each set of nerve roots and the sheaths are allowed to fill. Any filling defects should be recorded with anteroposterior and oblique spot films. After the fluoroscopy the iodized oil is maneuvered beneath the needle by tilting the table and is removed by suction applied to the needle.

Pennsylvania Medical Journal, Harrisburg

45:673-768 (April) 1942

Diagnosis and Treatment of Pituitary Disease. M. A. Goldzieher, New York.—p. 687.
Fertility in Male: Study of 132 Consecutive Cases. H. K. Sangree, Philadelphia.—p. 694.
Management of Idiopathic Ulcerative Colitis. K. A. Elsom, Philadelphia.—p. 697.
Problems in Surgery of Large Bowel. D. C. Geist, Philadelphia.—p. 701.
Treatment of Compound Fractures Involving Joints. J. W. Levering, Abington.—p. 705.
*Intestinal Manifestations of Milk Allergy in Newborn Period. M. I. Rubin, Philadelphia.—p. 711.
Staphylococcus Aureus Meningitis. R. H. Peters, S. S. Spector, E. L. Porter and H. Pleasants Jr., West Chester.—p. 715.
Malignant Tumors of Accessory Nasal Sinuses. N. S. Weinberger, Sayre.—p. 719.
Diagnosis of Giardia Intestinalis Infestation by Means of Intestinal Intubation: Treatment with Atabrine and Follow-Up Studies of Sixty-Eight Cases. Elizabeth Pennock Maris and Sarah Bushong, Philadelphia.—p. 724.

Milk Allergy in Newborn.—Rubin describes a syndrome in newborn infants which is a manifestation of milk allergy. In each of his patients there was a strong parental history of allergy; cow's milk feeding was started immediately or within a few days of birth, but hunger, or what the mother thought was hunger, was a constant complaint. This "hunger" probably represented abdominal discomfort manifested as "colic." Despite the abdominal distress, weight gain was not impeded. The "colic" first appeared about three weeks after feeding with cow's milk was begun and became progressively worse. Within a few days after its onset loose stools appeared, soon to contain mucus and bright red blood. The amounts of blood varied from small pinhead size clots to profuse hemorrhage containing no fecal matter. The blood disappeared from the stools within forty-eight hours after cow's milk was withdrawn from the diet. The mucus in the stools and the "colic" disappeared shortly afterward. In most of the infants diathetic eczema developed within a few months after the onset of the intestinal symptoms, and 2 infants have also had asthma. All except 1 infant tolerated goat's milk. Eggs, orange juice and cod liver oil, given at an early period, may also be offenders.

Texas State Journal of Medicine, Fort Worth

37:761-836 (April) 1942

Results of Treatment of Various Cardiac Mechanism Disturbances. G. M. Decherd Jr. and G. R. Herrmann, Galveston.—p. 767.
Air Embolism: Its Cause and Treatment. S. McDaniel, Houston.—p. 770.
Clinical Experiences with Coronary Thrombosis. G. Graves, Houston.—p. 773.
Iodized Oil in Chest Diagnosis. H. R. Hoskins, San Antonio.—p. 775.
Use of Wangensteen's Suction Apparatus and Enterostomy in Abdominal Surgery. B. B. Smith, Houston.—p. 776.
Use of Contrast Mediums in Uterus and Tubes. W. V. Ramsey, Abilene.—p. 780.
Postnatal Fibroma. F. P. Schuster and S. A. Schuster, El Paso.—p. 782.
Benign Mixed Tumor of Pharyngomaxillary Space and Related Area: Report of Case. B. Woodson, Temple.—p. 785.
Evaluation of Child Health Conferences. H. Wood, Austin.—p. 788.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

65:1-114 (March) 1942

Structure of Neurohypophysis, with Special Reference to Nerve Endings. E. Vazquez-Lopez.—p. 1.

Systemic Nervous Affinity of Triorthocresyl Phosphate (Jamaica Ginger Palsy). C. D. Aring.—p. 34.

Anatomy and Physiology of Cutaneous Sensibility: Critical Review. F. M. R. Walshe.—p. 48.

British Journal of Dermatology and Syphilis, London

54:99-128 (April) 1942

Moles and Malformations of the Skin in Their Relationship to Inheritance and Phylogenesis (New and Old Investigations): I. Conditions That Determine the Formation of Moles and Malformations of the Skin. E. Meirowsky.—p. 99.

Case of Hologynic Inheritance of Ichthyosis Vulgaris. T. Davies and D. McGregor.—p. 121.

British Medical Journal, London

1:377-402 (March 21) 1942

Technic for Filtration of Human Plasma and Serum for Transfusion. R. G. MacFarlane, J. C. Macsween, B. R. S. Mainwaring and H. J. Parish.—p. 377.

Thrombocytopenic Purpura Complicating Arsenobenzene Therapy. S. M. Laird.—p. 381.

*Treatment of Fractured Ribs. D. J. N. Smith.—p. 383.

Cardiac Massage. J. C. Nicholson.—p. 385.

Treatment of Fractured Ribs.—Smith relieved the pain of fractured ribs in 12 cases by injecting nupercaine around the fracture. Usually the sharp stabbing pain disappeared at once; in only 3 instances one other, and in 1 two other injections were required. The immediate disappearance of the sharp stabbing pain confirms the fact that it has its origin in the fracture. The patient was usually left with the less localized dull ache. The sharp pain did not return, although the action of the anesthetic could hardly have lasted more than twelve to twenty-four hours. However, the dull ache persisted for about ten days. In treating fractured ribs by this method injury to other structures or the development of a pleural effusion or hemothorax must not be overlooked. As the pain is relieved by one injection, some permanent change must take place: probably the relief of spasm, allowing the fractured surfaces to resume a normal position.

1:403-428 (March 28) 1942

Rehabilitation in the Royal Air Force. R. Watson-Jones.—p. 403.

Staphylococcus Albus Septicemia, with Reactions of 150 Strains of Staphylococci: Case. Mary Barber.—p. 407.

Presence of Diffusing Factor Among Metabolites of Aerobic Micro-Organisms. J. Ungar and A. L. Bacharach.—p. 409.

*Sterilization of Surgical Rubber Gloves. D. A. Sanford and H. A. Cookson.—p. 412.

Sterilization of Rubber Gloves.—The elimination of air from the sterilizing chamber, Sanford and Cookson find, with the steam at atmospheric pressure (0 pound) might effectively sterilize rubber gloves with less deterioration to them than under pressure. The cutting the pressure down to atmospheric level would subject the gloves to physical conditions similar to those of sterilization by boiling and yet the gloves would be dry at the end of the process.

1:429-458 (April 4) 1942

Child Health in Holland, England and Scotland: Sixty Years of Progress. C. McNeil.—p. 429.

*Treatment of Phosphorus Burns. E. W. Godding and H. E. F. Notton.—p. 433.

Relative Needs of Young Male and Female Rats for Vitamin A. Katharine H. Coward.—p. 435.

Puerperal Cerebral Thrombophlebitis Treated by Heparin. F. R. Stansfield.—p. 436.

Treatment of Phosphorus Burns.—Godding and Notton propose the following first aid treatment for phosphorus burns (after experiments in rats), which can be included as part of the soldier's standard equipment. First stage: Remove the bulk of the free phosphorus and superficial acid with alkali powder (formula 2_A, 10 per cent of heavy magnesium oxide, 5 per cent of borax and 85 per cent of sodium carbonate). Under no circumstances must liquid suspected of containing phosphorus be dabbed with a handkerchief or other dry material. If water has been used to extinguish the phosphorus, sprinkle the powder on to the wet surface, add more water if necessary, and work up to a medium thick paste, covering the whole of the burn and the surrounding area if contamination is suspected. Wash or wipe off and reapply as long as effervescence continues. Drying must be avoided at this stage. The advantages claimed over the official treatment are greater concentration and osmotic effect and the prevention of displacement of unignited phosphorus to other parts of the body or clothes. Second stage: Immobilize the whole of the remaining free phosphorus by the use of glycerin-copper sulfate paste (formula 3 or 4, 22.5 per cent of copper sulfate, 67.5 per cent of glycerin, 5 per cent of starch and 5 per cent of water or 20 per cent of copper sulfate, 40 per cent of glycerin, 7.5 per cent of starch, 1 per cent of sodium tauroglycocholate and 31.5 per cent of water). Apply sparingly but thoroughly, and rub well in. Remove by washing or wiping as soon as no smell of phosphorus is perceptible in the wound. The advantages claimed over the official treatment are concentration, rapidity, osmotic effect and completeness of action. Third stage: Neutralize the deep seated penetration of acid with alkaline powder (formula 2_A). Reapply the powder, work up to a paste with water, bandage and dampen the bandage occasionally. Do not allow bandages to dry. The importance of this stage has apparently not been previously recognized. Fourth stage: Remove to hospital labeled "phosphorus burn," where subsequent treatment should avoid all forms of coagulation therapy (tannic acid, picric acid, silver nitrate) in view of the obvious necessity for not "sealing in" the acid products. The painful nature of phosphorus burns and their tendency to delayed healing may possibly result from the inadequate treatment of the concentration of acid, and the alkalinity of the tissues may not be sufficient to deal with it. Therefore the continued treatment should be alkaline and might consist ideally of the envelop treatment with sodium hypochlorite solution.

Edinburgh Medical Journal

49:145-208 (March) 1942

Surgery of the Hypopharynx: Pharyngeal Pouch. J. M. Graham.—p. 145.

Id.: Postcricoid Carcinoma. J. M. Graham.—p. 164.

Popular Misconceptions in Connection with the Eyes. H. M. Traquair.—p. 179.

On Ossification and Vitamin D Action. J. P. McGowan.—p. 190.

Studies in Method and Standardization of Blood Examination: IX. Size and Site of Sample in Differential Leukocyte Count. S. Hay.—p. 200.

Lancet, London

1:373-404 (March 28) 1942

Army Physical Development Center. F. Howitt and A. Wesson.—p. 373.

Prognosis of Mental Instability—Adolescent and Service Cases. S. B. Hall and Muriel Barton Hall.—p. 376.

Salvaging of Fracture of Femoral Neck. R. Whitman.—p. 378.

*Minimal Requirements of Nicotinic Acid—White versus Wholemeal Bread. E. Kodicek.—p. 380.

Autodetoxication of Stilbestrol During Pregnancy. B. Zondek and Y. M. Bromberg.—p. 381.

Staphylococcic Food Poisoning Due to Contaminated Soup. G. C. Dorling.—p. 382.

Lumbar Sympathectomy in Treatment of Popliteal Aneurysm. R. L. Richards and J. R. Learmonth.—p. 383.

External Genital Hypertrophy in Infancy. H. Poston and A. H. Barber.—p. 384.

Minimal Requirements of Nicotinic Acid.—The minimal requirement of nicotinic acid sufficient to prevent pellagra in man is about 8 to 10 mg. daily. This amount, Kodicek points out, may not be enough to prevent subdeficiencies. White bread has little nicotinic acid, and the average current diet containing white bread furnishes a mean daily intake of about 9 mg. A diet with wholemeal bread would increase the daily intake to about 12.3 mg. The substitution of wholemeal or 85 per cent wheatmeal for white bread would thus render the supply adequate. Pellagra has been reported in northern Ireland.

Tubercle, London

23:1-24 (Jan.) 1942

Rehabilitation and Care of the Tuberculous: Fifth Report of the Employment Committee of the Joint Tuberculosis Council. P. Edwards, G. Jessel, D. P. Sutherland, F. R. G. Heaf and J. B. McDougall.—p. 1.

Schweizerische medizinische Wochenschrift, Basel

71:1573-1604 (Dec. 20) 1941. Partial Index

Impairment of Growth by Steroids and Hormone Specific Action: Problem of Spontaneous Tumors. W. von Möllendorff.—p. 1573.
*Pneumoperitoneum After Laparotomy. R. Imbach.—p. 1574.
Toxic Polyneuritis Caused by Sulfamethylthiazole. O. Gsell.—p. 1576.
*Treatment of Diabetes Mellitus with Gonadal Preparations. Anita Saurer.—p. 1577.
Roentgenologic Diagnosis of Early Exulcerated Primary Gastric Cancer and of Cancerous Degeneration of Ordinary Gastric Ulcer in the Early Stage. E. Walder.—p. 1585.
*Improvement of Carbohydrate Tolerance by Testosterone Propionate. L. Feil.—p. 1601.

Pneumoperitoneum After Laparotomy.—In the course of laparotomies air enters the abdominal cavity and some of it remains in the peritoneal cavity after closure of the abdomen. This air, according to Imbach, can be demonstrated clinically by a complete or partial obliteration of the hepatic dulness and roentgenologically by the presence of a crescentic shadow between the diaphragm and the liver. In the case of pressure changes in the abdomen this air exerts a tension stimulus on the sensory receptors of the phrenic nerve in the diaphragm and may elicit subjective sensations such as pain in the shoulder, piercing pain in the chest and a feeling of pressure under the sternum. These harmless manifestations may be mistaken for pulmonary infarct, particularly if a mild dyspnea exists, which is elicited by elevation of the diaphragm. Knowledge of the possibility of the presence of a pneumoperitoneum after laparotomy will clarify the significance of certain postoperative sensations in the region of the thorax and shoulder and give reassurance as to their harmlessness.

Gonadal Preparations for Diabetes Mellitus.—Diabetic disturbances frequently concur with disorders in the gonadal function. Saurer observed that, when gonadal preparations are administered to diabetic women passing through the menopause, not only do their menopausal symptoms improve but their carbohydrate metabolism is favorably influenced. She administered synthetic gonadal preparations to 17 patients with diabetes mellitus between the ages of 47 and 75. Men were treated with testosterone propionate and women with endocrine preparations of either sex. In cases in which regulation of menstruation is aimed at, estrogens are preferable, but in cases in which termination of the menopause is desired androgens may be given. In 15 cases medication with gonadal preparations was followed by an improvement in sugar tolerance. This was evidenced by a decrease in blood sugar values and by a lowering of the maximal elevation of the curves plotted from the results of oral dextrose tolerance tests (50 Gm. by mouth). The simultaneous control of the excretion of sugar in the urine likewise revealed a decrease in most cases. The curves of insulin tolerance tests (10 units subcutaneously) usually were lower after the treatment. The intravenous tolerance tests (8 Gm. of dextrose) resulted in almost normal curves. The carbohydrate metabolism of normal persons was not influenced by the administration of gonadal substances. There were no undesirable secondary effects. Cases exhibiting menopausal disturbances were improved by gonadal substances. In two cases abnormally high metabolic rates were reduced. High blood pressure, however, was never modified. The author suggests that gonadal hormones act on the carbohydrate metabolism of the diabetic probably by way of the anterior lobe of the pituitary. The gonadal substances are indicated particularly for diabetic patients of the menopausal age. In adolescent diabetic patients the action of hormones is not so well explained and undesirable secondary effects are possible. Oral medication of diabetes mellitus seems possible in some cases. Perlingual medication or perhaps implantation of crystals of the synthetic gonadal preparations are other possibilities in the future treatment of diabetes mellitus.

Improvement of Carbohydrate Tolerance by Testosterone Propionate.—Feil reports a case in which symptoms of hypertrophy of the prostate had been present for two years and diabetes for fifteen years. When the patient, a man aged 63, was given injections of testosterone propionate to counteract the prostatic symptoms, it was found not only that the urinary disturbances were benefited but that the carbohydrate tolerance showed likewise a surprising improvement.

Münchener medizinische Wochenschrift, Munich

88:1001-1028 (Sept. 12) 1941. **Partial Index**

Continued Traction on Fetal Head by Means of Weight as Auxiliary Force in Obstetrics. A. Döderlein-München.—p. 1003.
Scalp Forceps in Treatment of Arrested Delivery. E. Engelhart and S. Koehler.—p. 1005.
Female Psyche and Conception. B. Belonoschkin.—p. 1007.
*Action of Vitamin K in Menorrhagia and Metrorrhagia. R. Dietz.—p. 1009.

Action of Vitamin K in Menorrhagia and Metrorrhagia.—Dietz reports observations on 17 women with menorrhagia or metrorrhagia treated with vitamin K. So-called juvenile hemorrhages were present in 6 cases, in 5 of which good reaction occurred to vitamin K treatment; in the sixth case, however, menorrhagia recurred during the following menstrual period but was again successfully combated with vitamin K. In the second group there were 7 cases of polymenorrhea, 6 of which reacted favorably and 1 did not. The third group comprised 4 women with metrorrhagia in all of whom vitamin K counteracted the hemorrhages. On each of the first two days the women were given an intramuscular injection of 10 mg. of a vitamin K preparation, and this was followed by 2 tablets daily by mouth for five days. In spite of the limited number of cases and of the fact that the prothrombin level was not determined, the remarkable efficacy (only one failure in 17 cases) justifies further trials with this method.

88:1081-1100 (Oct. 3) 1941. Partial Index

Trauma and Nutritional Disturbances as Cause of Chronic Diseases of Bones and Joints. H. Augerer.—p. 1081.
*Action of Sulfathiazole on Artificial Fever. H. Nicolai.—p. 1084.
Experiments on Serologic Demonstration of Trichinosis and Their Clinical Significance. W. Schulz.—p. 1085.

Action of Sulfathiazole on Artificial Fever.—Nicolai demonstrated that sulfapyridine exerts a central, fever depressing effect. He found in recent experiments that sulfathiazole has practically no such effect. He concludes that, if fever declines after the administration of sulfathiazole, it indicates that the micro-organisms have been definitely counteracted.

Zentralbl. f. Gewerbehyg. u. Unfallverhütung, Berlin

28:57-88 (March) 1941

Results of Serial Physical Examinations in Industrial Concerns; Health Card Index of Health Department of German Labor Service. E. Zapel.—p. 57.
*Danger from Benzene to Vulcanizers in Tire Repair Workshops. K. Humperdinck.—p. 66.

Danger to Vulcanizers in Tire Repair Shops.—Humperdinck describes the procedure in tire repair shops and directs particular attention to the solvents and rubber solutions. These, as a rule, are specialties of different firms. Analysis of one rubber solution revealed 93 volumes per cent of aliphatic hydrocarbons and 7 volumes per cent of aromatic hydrocarbons. Another rubber solution was found to contain 63 volumes per cent of aliphatic and 37 volumes per cent of aromatic hydrocarbons. The solvents used were a special benzine, 90 per cent commercial benzene and pure benzene. The special benzine contains up to 14 per cent of aromatic hydrocarbons. The 90 per cent commercial benzene contains from 80 to 85 per cent of benzene and benzene homologues (xylene and toluene). The author investigated 9 different tire repair shops in order to determine to what extent the vulcanizers and helpers are endangered by benzene in their contact with rubber solutions and solvents. Although well developed chronic benzene poisoning was not encountered, workers most exposed to benzene exhibited predisposition to hemorrhages, a relative lymphocytosis and high absolute lymphocyte values, in addition to considerable subjective complaints. The investigations disclosed better results in shops using special benzine. The following recommendations were made for the protection of the workers: Special benzines should be used instead of benzene; the workrooms should be suitable and the work should be properly arranged; the workers should be subjected to prophylactic examinations, and care should be taken that their diet is adequate, particularly with regard to vitamins and more especially to vitamin C.

Book Notices

The Treatment of Burns. By Henry N. Harkins, M.S., M.D., Ph.D., Associate Surgeon, Henry Ford Hospital, Detroit. Cloth. Price, $6.50. Pp. 457, with 117 illustrations. Springfield, Illinois & Baltimore: Charles C Thomas, Publisher, 1942.

Dr. Harkins has written a remarkably good book on burns. In this monograph the author covers practically every phase of this difficult subject in a scholarly fashion. In correlating clinical practices with experimental studies, he has reviewed the literature exhaustively. His discussions of the voluminous research and experimental work on burns are presented in an orderly and critical but impartial manner. The bibliography will be most valuable to any one interested in the study of burns. The author quotes from the literature so freely that the book is not always easy reading. The impartial reporting of apparently conflicting views of other authors may be confusing to some readers. There will, of course, be differences of opinion as to whether the author has always given credit and emphasis fairly in his surveys as to the progress of knowledge on this complex subject. This, however, does not impair the value of his book.

Part I discusses the burn and its effects, giving an introduction followed by chapters on pathology, chemical changes, blood concentration, burn shock, the adrenal glands, fluid loss, the role of toxins, the role of bacteria, early complications of burns, Curling's ulcer and late complications of burns. In general, the discussions in this part of the book are excellent. The chapter on pathology is interesting and instructive, as likewise are the chapters on shock, the role of the adrenal glands and the role of bacteria. The voluminous complications of burns are presented in an orderly manner. There is little to criticize. It does seem that more could be said in the chapter on blood chemical changes. These are extremely variable in burns, but there is evidence in the literature that many of these conflicting findings may be explained on the simple hypothesis that blood chemical changes in severe burns will vary depending on the amount and the character of the fluid given and how the patient is handling it. Strangely, the book gives no discussion of this important consideration. Similarly, the chapter on the role of fluid loss seems not to include all the recent advance in knowledge on disturbances of fluid balance in burns. Concerning the role of toxins, the author discusses the well known fact that some patients, especially young children, whose burns do not appear dangerously extensive will die rapidly with a peculiar intoxication which for a want of a better term has been called "acute toxemia." Dr. Harkins gives an excellent review of this problem, emphasizes the fact that modern therapy has not solved it, and leaves the subject open.

Communicable Disease Nursing. By Theresa I. Lynch, R.N., Ed.D., Instructor in Education, New York University, New York. Cloth. Price, $3.75. Pp. 678, with 161 illustrations. St. Louis: C. V. Mosby Company, 1942.

This substantial book is intended not only to present the technical phases of communicable disease nursing as taught and practiced today in modern hospitals but also to show the part the nurse may play in the community in aiding in the prevention and control of such disease. The author, who was formerly director of instruction and then superintendent of nurses at the Willard Parker Hospital in New York City and who is now instructor of education at New York University, has had a considerable teaching experience and has also apparently had the advantages of the advice and assistance of many well informed people in the preparation of this book. As a result, a book of much value has been achieved.

The six chapters of part I are devoted to general discussions which will help to orientate a nurse to the nursing of communicable diseases. Then follow chapters discussing some sixty-six infectious diseases, brief discussions being given of the respective illnesses and more extended accounts of the nursing care. A useful chapter on home care follows, together with a number of appendixes and a glossary. Each chapter has an appended list of references, usually textbooks. The volume is profusely illustrated with photographs largely of nursing procedures, almost redundantly so. For instance, there is a series of thirty-eight half page photographs of the Willard Parker Hospital nurses' gown technic, a technic which has been changed in some details since these photographs were taken. Five colored plates are borrowed from other textbooks, one supposed to illustrate the eruption of scarlet fever showing a most atypical involvement of the face.

It is doubtful whether pupil nurses will find the descriptions of the diseases sufficiently informative for their needs, so that the book will probably prove more valuable as a reference book than as a textbook. As is bound to occur in all new books, a number of outdated items have crept in, such as the table on page 163 worked out by Park a number of years ago. In the glossary, the definition of virus as "any toxic agent capable of producing disease; a micro-organism or its toxin" is hardly acceptable. The infectious period of chickenpox is considered on page 137 as approximately two weeks, although most public health authorities now believe it is not much longer than a week. On page 119 we read that, because Broadhurst's inclusion bodies are abundant even on the fourteenth day of the disease, carriers may play a part in measles transfer, a statement that might well have been omitted. Throughout, the paragraphs on differential diagnosis amount only to lists of possibly similar illnesses. On the whole, however, the book is valuable and should be available to all student nurses.

Surgery of the Ambulatory Patient. By L. Kraeer Ferguson, A.B., M.D., F.A.C.S., Lieut.-Commander, Medical Corps, United States Naval Reserve. With a section on Fractures by Louis Kaplan, A.B., M.D., F.A.C.S., Associate in Surgery, University of Pennsylvania, Philadelphia. Cloth. Price, $10. Pp. 923, with 645 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1942.

There has long been a need for a textbook on the treatment of surgical conditions in ambulatory patients. The need has now been fulfilled by this author in more than an adequate and satisfactory manner. On the basis of a large personal experience, he discusses thoroughly the surgical conditions most frequently encountered that can be treated in a physician's office or in an outpatient surgical clinic without hospitalizing the patient. The book is divided into three parts. The first part covers general surgical problems, principles and lesions, such as equipment, anesthesia, infection, foreign bodies, preparation and conduct of operations, postoperative care, foreign bodies and the treatment of wounds. The second part deals with regional surgery. In this section are considered the common surgical conditions of the various parts of the body and the methods of their treatment. In the third part Dr. Louis Kaplan, the author's associate, excellently covers the subject of fractures and dislocations and their modern treatment. The book is written in clear language and is easy to read. It is concise, yet contains a vast amount of useful and practical information. In the treatment of the various conditions, the methods and technics are described with distinct details. The steps leading to success as well as possible errors and dangers are pointed out. A large number of photographic reproductions, diagrams and line drawings enhance the clarity of the text. On the whole it is an excellent book which is a valuable addition to the surgical textbooks and literature. It is highly recommended for study and reference to the younger men and general practitioners for whom this work is intended.

Perineopelvic Anatomy from the Proctologist's Viewpoint. By R. V. Gorsch, A.B., M.D., Adjunct Professor of Proctology, New York Polyclinic Medical School and Hospital, New York. Cloth. Price, $8. Pp. 298, with 157 illustrations. New York: Tilghman Company, 1941.

This monograph on the anatomy of the perineum and pelvic organs is an attempt to provide a good anatomic background for clinical problems in this special field. The author feels that a more thorough understanding of the anatomy will lead to more rational and better therapy. The perineum, including muscles and fascias, are described and profusely illustrated by means of diagrams and dissections. The anatomy of the anus, rectum and sigmoid is illustrated in detail by the use of histologic and gross preparations. Some attempt is made to show the relationships between these structures and other environmental viscera, such as the reproductive organs, but more stress could be placed on this relationship. The lymphatic, nerve and blood vessel supply of the pelvic structures is well presented. This volume is a valuable addition to the library of the proctologist and gynecologist.

The Physiology of Domestic Animals. By H. H. Dukes, D.V.M., M.S., Professor of Veterinary Physiology, New York State Veterinary College, Cornell University, New York. With a chapter on the Physico-Chemical Basis of Physiological Phenomena by E. A. Hewitt, D.V.M., Ph.D., Associate Professor of Veterinary Physiology, Division of Veterinary Medicine, Iowa State College; a part on the Endocrine Organs and Reproduction, revised by S. A. Asdell, M.A., Ph.D., Professor of Animal Physiology, New York State College of Agriculture, Cornell University; and a foreword by H. D. Bergman, D.V.M., Professor of Veterinary Physiology and Pharmacology, Division of Veterinary Medicine, Iowa State College. Fifth edition. Cloth. Price, $6. Pp. 721, with 168 illustrations. Ithaca, N. Y.: Comstock Publishing Company, Inc., 1942.

A review of the forth edition (THE JOURNAL, Jan. 8, 1938) commented on the dearth of comparative physiology of domestic animals, a defect that has been partly corrected by inclusion of "a chapter on digestion in the chicken and sections on respiration in birds, urine of the chicken, reproduction in the fowl, and physiological oxidations" (quoted from author's preface). The revised tables on comparative composition of the blood of eight species of domestic animals contain a wealth of information. Illustrative material has not been altered greatly. The style is smooth and entertaining, and adequately explanatory. Despite the good features of the book, the present reviewer agrees with the review of the fourth edition that there still appears to be a dearth of material on the special physiology of the different species of domestic animals. Some of these features actually receive more consideration in textbooks of human physiology. For specific comparative data there is an abundance of source material in special monographs that has not been incorporated in the text. Possibly some of this material is presented in other courses for veterinary students, but the reviewer feels some disappointment that it has not been synthesized in this book. However, it must be admitted that this is the most complete and satisfactory textbook on physiology available to the veterinary medical profession.

Endocrinology: Clinical Application and Treatment. By August A. Werner, M.D., F.A.C.P., Assistant Professor of Internal Medicine, St. Louis University School of Medicine, St. Louis. Second edition. Cloth. Price, $10. Pp. 924, with 328 illustrations. Philadelphia: Lea & Febiger, 1942.

This represents a substantial enlargement by about 40 per cent over the first edition of the work. There is provided some extensive discussion of the anatomy and physiology of the autonomic nervous system, the endocrine organs and detailed discussions of each of the glands of internal secretion and of several metabolic processes which are in part endocrine problems in the clinic. The style is essentially conversational rather than being a rigorously organized dissertation. The illustrations include diagrams, photomicrographs and numerous photographs of typical patients. The work of this author represents a transition from the diagnostic classifications based on skeletal types and the disposition of subcutaneous fat to the more exact diagnoses based on measurements and the laboratory methods for quantitative determinations of biologic process. Therapy is discussed frankly, and there is an attempt to use the names of commercial preparations and also to use the general names of types of hormone containing extracts. A considerable degree of documentation of the volume makes it of interest to the detailed student in the field. An extensive index of subjects and also one of the authors adds materially to the usableness of the volume.

Minor Surgery. By Charles M. Oman, M.D., F.A.C.S., Rear Admiral, Medical Corps, U. S. Navy. Cloth. Price, $2. Pp. 165. New York, Toronto & London: Oxford University Press, 1942.

This small volume is unique. It is one of a series of medical outlines published by the Oxford University Press; the entire work, consequently, is written in complete sentence outline form. The important points of the various conditions generally included under the heading of minor surgery, with which the student and general practitioner should be familiar, are covered briefly, clearly and quite adequately. The subject matter discussed is extensive, including most conditions encountered which may be treated in an outpatient clinic or in a physician's office. Between the printed pages of the text are blank pages for additional notes. The work makes no pretense of being a textbook. It is what it was intended to be: a practical working guide, useful to students, practitioners and instructors.

Do You Want to be a Nurse? By Dorothy Sutherland. Cloth. Price, $2. Pp. 186. Garden City: Doubleday, Doran & Company, Inc., 1942.

This book is a concise, accurate and helpful and readable statement of what nursing is and what it takes to be a nurse. This being the stated purpose of the book, it can be considered a successful effort. The opportunities in nursing, according to its various branches and ramifications, including the growing specialties of public health and industrial nursing, are well described, often by brief summarized histories of typical nursing careers, presented under fanciful names. The book is neither discouraging nor unduly optimistic. It does not hide the fact that it is a hard job to get to be a good nurse, but that, like everything else worth having, it is worth the effort when you get there. Expect no fabulous wealth from nursing, but many satisfactions. As for nursing as a door to romance—evidently this is so lightly regarded these days that it is not even worth serious discussion in a book of this kind. Physicians who are asked to advise girls about nursing as a career, and about intelligent choice of a training school, may safely recommend this excellent book as at least one source of sound advice, pleasantly administered.

A Woman's Health. By William C. Danforth, M.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. Cloth. Price, $2.50. Pp. 398, with 9 illustrations. New York & Toronto: Farrar & Rinehart, Inc., 1941.

This is an admirable book. It provides a woman with sound advice on the gynecologic and obstetric phases of her health. It is written authoritatively, clearly and not too briefly. The author's advice is just about what would be given by any good physician. Many of the bugaboos of folklore are dispelled, much of current wisdom is included. Few personally prejudiced views can be found. Almost everything which a woman ought to know about her health as a woman is included. Among the subjects discussed are anatomy of the pelvis, physiology, disorders of menstruation, diet, marriage, fertility, obstetric care, feminine hygiene, venereal diseases, benign and malignant tumors, hormones and the menopause. The book should be read by every intelligent woman in the land. It is precisely what is needed and cannot be too strongly recommended.

Symptoms in Diagnosis. By Jonathan Campbell Meakins, M.D., LL.D., Professor of Medicine and Director of the Department of Medicine, McGill University, Montreal. Cloth. Price, $4. Pp. 323, with 62 illustrations. Boston: Little, Brown & Company, 1941.

This book is unusually well written and covers an extensive comprehensive subject in admirable fashion. It clearly demonstrates the physiologic mechanisms behind clinical manifestations, and on the basis of this the author arrives at a sound and scientific diagnosis. It is impossible in the space allotted to cover all diseases which one would encounter in the practice of medicine, nor does it specifically cover any one condition; such was not the author's intention. This book is to be highly recommended for both student and practitioner and will be found exceedingly useful to the specialist as well.

Neuro-Anatomy. By Walter R. Spofford, B.S., Ph.D., Instructor in Anatomy, Vanderbilt University Medical School, Nashville, Tenn. Cloth. Price, $2. Pp. 110. New York, Toronto & London: Oxford University Press, 1942.

This book presents a brief outline, such as a good student might prepare for himself while taking a course in neuroanatomy. Such an outline would be of great value to the student who made it because it would serve to organize the information he had acquired. It would help other students who had taken the same course to pass an examination. But because of its brevity and the absence of illustrations it would probably be of little value to any one else. There is a brief bibliography of twenty-seven references.

Harvard College Class of 1881 Fiftieth Anniversary. Cloth. Pp. 535. Cambridge, 1931.

The date of publication of this book is 1931. It was received in this office a few months ago. The book contains a roster of the class of Harvard College of 1881, together with a brief biography of each member, living and dead. The roster is notable for the preponderance of family names which any one would recognize as those of pioneer families.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ARSENICAL PREPARATIONS AND MALARIA

To the Editor:—**For years my associate and I have controlled malaria in syphilitic patients with the injection of neoarsphenamine. I had 1 patient with chronic malaria, nonsyphilitic, with a large spleen, who had taken quinine for ten or twenty years with recurrent attacks, which was cleared up by two intravenous injections of arsenicals. I have noticed in the literature all sorts of articles on the treatment of malaria with quinine but never any with the arsenicals. Is it possible that the treatment of malaria with arsenicals is not generally known to the profession?**

M.D., California.

ANSWER.—For more than a quarter of a century physicians have tried arsenical preparations as antimalarials, especially for quinine resistant patients. All clinical authorities on the subject (American, British, Dutch, German, French) are agreed that arsenicals per se apparently have little, if any, plasmodicidal action, even in benign tertian malaria, for which these drugs have at times been enthusiastically advocated. The record has been similar with solution of potassium arsenite, sodium cacodylate, arsphenamine, acetarsone, neoarsphenamine and mapharsen: arsenicals have proved entirely useless in quartan and falciparum malaria, but they have been reported to have malaricidal properties against the tertian parasite. In conjunction with cinchona derivatives or atabrine, arsenicals have probably been useful adjuvants in providing clinical cure for patients suffering from chronic malaria.

As far as it is possible to provide an evaluation, the efficacy of arsenicals in malaria is confined to their tonic action. Together with the feeding of absorbable iron to build up hemoglobin, adequate nourishment and a stimulating climate, the administration of arsenicals in conservative amounts may help the patient to develop an adequate defense mechanism against the reservoirs of malaria parasites in the spleen, bone marrow and other centers not always reached by quinine or atabrine.

It may be concluded that the hopes that arsenicals might prove to be satisfactory alternatives for quinine in their direct action on the malaria parasites have not been fulfilled. Their action is adjuvantal, and as such their usefulness should neither be minimized nor overrated.

BRONCHIECTASIS

To the Editor:—**A white man aged 54 had a rib resection in 1916 for abscess of the right middle lobe. From the history, I believe this also perforated into the bronchus. Since that time he has been well except for attacks of coughing, which are accompanied by considerable sputum and bright blood. At present he has been coughing for about two months. The cough is productive, mostly at night, and blood is present almost all the time. Roentgenograms show no evidence of tuberculosis or other gross lesion. Sputum is negative for tubercle bacilli but is described as characteristic of bronchiectasis. One chest man feels that iodized oil should be injected and then roentgenograms taken; another feels that this is contraindicated because of the probable diagnosis of bronchiectasis. Should this be done? Is bronchoscopy indicated? Your opinion will be appreciated.**

M.D., New York.

ANSWER.—If one assumes that this patient had an abscess of the lung, it is reasonable to assume now that he has a bronchiectasis in the site of the former abscess. This is a common sequence of events, and this probability is strengthened by the fact that his coughing comes in attacks and that the roentgenograms do not show evidence of any gross lesion. Bronchiectasis is one of the few lung conditions which can produce symptoms without important x-ray apparatus. The only way of being sure of the diagnosis of bronchiectasis would be by taking roentgenograms after the injection of iodized oil into the affected area. This is a safe procedure and appears to be definitely indicated. Bronchography is routine in cases suggestive of bronchiectasis. The presence of blood in the sputum is common. In a man 54 years of age it always leads one to think of cancer. Occasionally cancer develops on the basis of some chronic bronchial or pulmonary disease, although the long history and the absence of gross x-ray appearances are against cancer. A small intrabronchial lesion could conceivably be present. Bronchoscopy, on the other hand, is a safe and simple procedure and in this case would be of additional value in determining precisely from which bronchial units the pus and blood come.

Operations are commonly performed on a mistaken diagnosis of lung abscess. This was much more common in 1916 than it is today. One of the common conditions mistaken for lung abscess is a localized empyema which has broken into the bronchus. If this fails to heal completely following drainage, the patient may continue to cough and expectorate pus from a small chronic empyema cavity for many years without showing any signs of sepsis. Other rare causes of chronic cough and expectoration are collections of pus beneath the diaphragm, either in the liver or in the subdiaphragmatic space, which have penetrated the diaphragm and broken into the lung. When this happens there are often no important pulmonary or pleural findings, and the conditions may become very chronic and persist for many years.

In this case bronchiectasis seems to be the most probable diagnosis. Bronchography is indicated and perhaps bronchoscopy. Both are likely to give important information, and neither is likely to do harm.

RECURRING PLANTAR WARTS

To the Editor:—**I am a physician aged 29; I am in excellent health and have no complaints except plantar warts. Since 1938, when my warts started while I was a medical student, I have been under active treatment by competent dermatologists. The first single wart was on my right heel and was treated with radium. It disappeared for several months and then returned. It was next treated with a massive dose of radium—so large a dose that a small piece of skin and tissue sloughed out. In 1939 the same wart returned—each one being the same "black seedy" type. While I was interning another dermatologist used roentgen rays repeatedly and the wart disappeared again, only to reappear a few months later but this time in a different place and almost a "crop." Another dermatologist recommended injections of a bismuth compound and another by mouth and this was tried for several months until my stomach revolted from the bismuth. This didn't help, so for several months 20 per cent salicylic acid plasters were used without success. At the present time they have spread to the bottoms of both my feet and walking is becoming difficult. The dermatologist is now injecting a bismuth compound into the base of each wart and this also has been unsuccessful; in fact, from my handling them I now have a wart on the margin of my thumbnail and I'm afraid that perhaps by cleaning my fingernails I'll spread warts to all my fingers. My dermatologist and I would greatly appreciate any other suggestions.** **M.D., Utah.**

ANSWER.—Although the great majority of warts yield to comparatively mild treatment, histories such as this are heard too frequently for the complacency and self esteem of the dermatologist. In certain cases even after rigorous treatment such as the radium attack recorded in the query, or deep cauterization, the wart may recur. The reason for this great variation in susceptibility to treatment is not known. The thickness of the epidermis on the soles is one factor and perhaps the daily irritation of walking. Similarly incorrigible warts are encountered on the palms and on other parts with still thinner epidermis, but rarely. The new "almost a crop" during the internship was of course not a recurrence but the result of a new infection. This and the one on the thumb are evidence that insufficient precautions have been taken against autoinfection. In all manipulation of the infected areas, surgical precautions must be observed. Oozing of serum or blood from the warts should be avoided whenever possible, and if it does occur it should be regarded and treated as infectious. The results of such infections are very slow to appear, seldom being seen within a month and sometimes delaying for many months. Cleansing the thumb nail in the vicinity of the wart must be done with surgical precautions against infection, the instrument employed being sterilized before being used elsewhere. Picking at warts is strictly forbidden.

A recent contribution to the literature of the subject is by Karp and Frank (Electrosurgical Removal of Plantar Warts, *Arch. Dermat. & Syph.* **45**:328 [Feb.] 1942), who use a specially small cutting loop, made by twisting a larger one until the loop is reduced to 2 mm. in diameter and has a stem 8 mm. long. Under procaine and epinephrine anesthesia, this is inserted into the sole so deeply that the loop is wholly buried; then it is rotated on its axis a half turn, 180 degrees and withdrawn through the linear cut of insertion. Surgical precautions against infection are observed. Bleeding is slight and pain is minimal; in fact, preexisting pain disappears in most cases. During the eleven years in which it has been in use, this method of treatment has succeeded in 19 of 21 cases. This percentage of success is about that of other methods. The exponents of this method acknowledge that their operation does not remove all infected material. The 2 cases in which it failed were previously treated by other methods without success. This is in accord with the failures after other methods of treatment.

In a case such as the one cited in the query, in which all methods have failed, the chief desideratum is the comfort of

the patient. Protection against autoinfection is also important. Mild treatment, such as superficial cauterization once every week or two with reduction of the lesions enough to prevent pain from pressure, is just as likely to result in cure as energetic attacks, and much less likely to cause pain and incapacitation. Further irradiation with roentgen rays or radium should be avoided, certainly on the heel on which the severe reaction occurred.

If the patient can be kept comfortable and free from further infection, the warts may disappear at some time in the future.

SALYRGAN IN ACUTE NEPHRITIS OF CHILDREN

To the Editor:—A boy aged 4, with acute nephritis of two days' duration following a mild upper respiratory infection, developed edema of the eyelids, scrotum and lower extremities. There was marked ascites, vomiting, a temperature of 102 F. and inability to flex the spine. The patient had a similar attack four months previously, at which time a twin brother afflicted with the same disease died. The patient was seen at 11 a. m. and was given ammonium chloride solution by mouth and 0.5 cc. of salyrgan intravenously. The ampule of salyrgan was covered with cotton and placed on the table. The patient was seen again at 9 p. m., at which time stupor had disappeared, the swelling had slightly decreased and the patient appeared to be improved and was continuously requesting water. However, urine passed since the intravenous injection was less in amount than previously and contained a considerable amount of pus. The remainder of the ampule of salyrgan, which amounted to 1.5 cc., was given to the patient intravenously. Immediately after removal of the needle, the patient had a tonic convulsion and died. Epinephrine into the heart and artificial respiration with a mechanical resuscitator were of no avail. Postmortem showed the kidneys to have fetal lobulations and to be enlarged in size, the capsule stripped with great facility, the pelves contained purulent exudate. The abdomen contained about 2 quarts of yellow ascitic fluid. Although salyrgan is contraindicated in acute nephritis, it was given in this case for the ascites. Did death result from an overdose of salyrgan, from some toxic quality of the salyrgan standing in an open ampule for nine hours, or because it was contraindicated in this type of disease? If death was due to salyrgan should its result be so immediate? M.D., Arizona.

ANSWER.—It is not possible to judge from the history given whether or not this patient actually had an acute hemorrhagic nephritis of the postinfectious type, as there was no mention made of blood in the urine. Assuming that it was that disease, however, one would not ordinarily expect salyrgan to be efficacious in its treatment. There are several cases reported in which this identical sequence of events has happened; namely, after one injection of salyrgan with no difficulty, a second or third injection caused death. As far as is known, death in such instances is due to sensitivity to the drug. The death probably did not result from an overdose of salyrgan, or from any toxic quality following standing. The contraindications to the drug in this type of disease are that it is ineffective and that it sometimes causes this sort of accident.

HYPERTENSION AND INCREASED METABOLISM

To the Editor:—An automobile mechanic aged 32 was turned down by the draft board because of high blood pressure. He had been working every day and did not know that he was sick. His height is 5 feet 10 inches (178 cm.), weight 231 pounds (105 Kg.). He has not lost weight recently. His past history is negative except for a sickness in childhood which left a valvular lesion of the heart. The heart is well compensated and has never caused him any trouble. Blood pressure reading on an aneroid instrument was approximately 340 systolic and 160 diastolic. This was checked with two mercury instruments. A week later a reading of approximately 400/180 was obtained. Ten minutes after a dose of 1/100 grain (0.00065 Gm.) of glyceryl trinitrate the reading was 280/115. The basal metabolic rate is plus 42. He eats and sleeps well. The urine is normal. There are no other symptoms of hyperthyroidism. I am attaching a newspaper clipping which the patient brought to my office for my opinion. I would like your comment on it, as well as your suggestions for the treatment of this patient. He is taking iodine and a vasodilator and is in bed. D. W. Davis, M.D., Akron, Ohio.

ANSWER.—The occurrence of an elevated basal metabolic rate with obesity is far more common than is generally realized, for the usual "textbook" picture of hyperthyroidism places weight loss among the most characteristic symptoms. Excessive food consumption is frequently secondary to the appetite stimulation of hyperthyroidism; if this exceeds the catabolic increase, weight is gained. Eating to excess also becomes a habit to quiet the nervous tension and apprehension too typical of the syndrome. Eating is a sedative. These overweight patients may or may not show hypertension. Rarely is the diastolic tension conspicuously elevated unless there is preexisting or coincident hypertensive disease etiologically independent of the thyroid disorder. The response of the diastolic tension to vasodilatation with glyceryl trinitrate indicates that the hypertension is relatively recent or greater arteriolar rigidity would have been observed. The one determination, ten minutes after the administration of glyceryl trinitrate, does not necessarily reveal the full extent of the fall in pressure; many and frequent postvasodilator determinations are necessary to be assured that the minimum diastolic tension has been actually observed. Such extreme variations in tension as are mentioned in the query suggest some acute vasodepressor causation.

Before it is possible to make sound therapeutic suggestions for this patient it is necessary that further diagnostic study be carried out. Repetition of a vasodilator test either with glyceryl trinitrate or with amyl nitrite (Stieglitz, E. J.: Evaluation of the Prognosis in Arterial Hypertension, *Arch. Int. Med.* **46**:227 [Aug.] 1930) is indicated. Thorough study of the renal functional capacity, data on the blood picture, closer study of the heart and recheck of the basal metabolic rate are all needed. In view of the youth of the patient and the apparently adequate compensation of his heart, the possibility of coarctation of the aorta should be ruled out. This is readily accomplished by determining the arterial tension in the legs (popliteal fossae); a pressure lower in the legs than in the arms is pathognomonic of aortic coarctation. Unilateral renal disease with ureteral obstruction or polycystic kidneys may exist though a voided specimen of urine is "normal"; further investigation of such a possibility should most certainly be undertaken. Despite the present absence of headaches and conspicuous neurologic symptoms, there remains the possibility of brain tumor as a source of the hypertension. Because logical therapy to control must be highly individualistic and the program of management depends largely on specific etiologic factors, more thorough diagnostic study must precede formulation of treatment.

The therapeutic use of radioactive iodine, as mentioned in the newspapper clipping, is still purely experimental. Though this approach appears to offer some hope for the future in controlling certain metabolic disorders, it is far too early to venture predictions either as to its value or as to its hazards. Without adequate and careful control, administration of activated compounds is unwarranted. It is doubtful whether the elevated metabolism (as evidenced by a single uncorroborated determination) is a major etiologic factor in this patient's serious arterial hypertension. Adrenal neoplasm is a very rare but is a more probable cause than the hyperthyroidism.

A PROBLEMATIC POST-TRAUMATIC CEREBRAL SYNDROME

To the Editor:—Many varied symptom complexes follow brain injury. Recently a local Selective Service board was ordered by superior authority to classify a selectee as 1-B (qualified for limited military service) because of "post-traumatic cerebral syndrome." I can find no reference to such a clinical entity in the medical literature at my command. A detailed physical and neurologic examination by four medical members and one dental member of the board failed to reveal any abnormal physical signs or symptoms. No evidence of psychoneurosis or psychosis was found. The man indulges in strenuous physical activity daily. He had a skull fracture in 1939 from which he apparently has recovered completely. He states that he is now sound and well. Please supply any available information. Paul D. Luckey, M.D., Connellsville, Pa.

ANSWER.—By "post-traumatic cerebral syndrome" is usually meant a rather constant group of symptoms which not infrequently follow craniocerebral injuries. The most prominent of these symptoms are headache and giddiness, which are frequently precipitated by physical exertion or by stooping over. In addition these patients are often irritable and complain that their memory is poor, that they are unable to concentrate and that use of their eyes, as for reading or in a motion picture show, produces a feeling of "eyestrain" and headaches.

The condition is largely subjective, and it is not uncommon for detailed physical and neurologic examinations to reveal no significant abnormalities. This condition has been described in two recent books (Diagnosis and Treatment of Head Injuries, by S. W. Gross and William Ehrlich, New York, Paul B. Hoeber, 1940, and Injuries of the Skull, Brain and Spinal Cord, edited by Samuel Brock, Baltimore, Williams & Wilkins Company, 1940).

It is difficult to understand how any one could have made a diagnosis of "post-traumatic cerebral syndrome" or of any syndrome on a man who presented no symptoms of any sort but who, on the contrary, is "sound and well" and "indulges in strenuous physical activity daily." The mere fact that he sustained a fracture of his skull in 1939 is not sufficient basis on which to entertain such a diagnosis.

If the facts as stated in this inquiry are accurate and complete, the patient in question does not suffer from a "post-traumatic cerebral syndrome."

DRUGS FOR ARTHRITIS

To the Editor:—**I should like to have a fairly complete list of the drugs that are being used for the treatment of arthritis and an opinion as to the worth of each.**

M.D., Kansas.

ANSWER.—Scores of drugs are being used in the treatment of various types of arthritis. Many of them have little or no rationale. Some of them are designed to relieve pain, others (for example sulfur, vitamins) have been prescribed to correct some supposed (but unproved) deficiency; still others (for example gold salts) are being used to kill some supposed (but unidentified) type of infection. The sulfonamides have been found to have no beneficial effect in cases of rheumatic fever or in rheumatoid arthritis or osteoarthritis. The use of sulfonamides should be confined to the treatment of the specific arthritides of known bacterial origin (gonorrheal, staphylococcic, hemolytic streptococcus and so on). Vitamins in massive doses have not been proved to be of any notable value in cases of chronic arthritis, despite advertising ballyhoo. Acetylsalicylic acid continues to be the safest and generally the most effective analgesic drug and should be prescribed fairly generously, provided patients receiving it do not rely on it alone, thereby omitting other more important remedies. Opinions as to the use of gold salts for rheumatoid arthritis continue to differ notably. Some physicians of wide experience consider chrysotherapy "the remedy of choice"; others use it only when other remedies have failed; still other physicians have concluded that its toxic reactions outweigh its therapeutic value. A synopsis of current opinions on the worth of these and many other drugs for arthritis and rheumatism will be found in the Eighth Rheumatism Review (*Ann. Int. Med.* **15**:1002 [Dec.] 1941).

AIRPLANE "DOPE" AND ERYTHEMA NODOSUM

To the Editor:—**A woman aircraft worker aged 35, employed in painting "dope" on the wings of airplanes, has had lesions characteristic of erythema nodosum for two weeks. This substance is applied by brushing. The lesions have been on the right hypothenar eminence, both thighs and the midpretibial regions. Those on the hand and thighs have disappeared. The question has arisen whether or not this woman's occupation has anything to do with the skin condition. Certain drugs are known to cause similar lesions. So-called dural poisoning is common knowledge among the workers themselves. Do you have any explanation for this condition?**

M.D., California.

ANSWER.—"Dope" consists of cellulose nitrate, solvents and plasticizers. The solvents, when applied to the skin in sufficient quantity and for a sufficient length of time, as they would be if the hands are continuously immersed in them, would cause dermatitis of the parts exposed but would not pick out one particular small area such as the right hypothenar eminence.

The U. S. Public Health Service has made a study of dermatitis among airplane workers (Schwartz, Louis, and Russell, John P.: Skin Hazards in Airplane Manufacture, *Pub. Health Rep.* **56**:1581 [Aug. 8] 1941, reprint 2300) and found that the name "dural poisoning" was applied by workers to any cutaneous disorder from which they suffered. Patch tests were performed with duralumin and with Dow metal. They were found to be nonirritating. It is common practice for workers to put the blame on their occupation for any cutaneous disorder which they may have; for instance, rubber workers have "rubber itch," brass workers have "brass itch" and fur workers have "fur itch." Schwartz and Russell describe all skin hazards in airplane manufacture as the result of examinations of workers and working conditions made in nine airplane factories. They do not state that any such condition was found such as that described.

LEAD PENCIL MARKINGS ON FOOD PRODUCTS

To the Editor:—**What are the possible deleterious effects of the use of an indelible pencil in marking food products directly on the product itself? For instance, if on a turnip the weight should be placed on the product and was not removed during the cooking process, what, if any, ill effect is possible or probable? If you can, I would like to have a formula of the ingredients used in the so-called indelible lead.**

Ralph H. Wheeler, M.D., Chicago.

ANSWER.—There are many formulas for the indelible lead of pencils, a typical one being methyl violet 33 per cent, graphites 47 per cent, gum tragacanth 3 per cent and china clay 17 per cent. Practically all violet indelible pencils utilize methyl violet. For other colors, such as red or yellow, there may be employed magenta and aurimine as the pigment agent, with other constituents remaining much the same. In the case of methyl violet it is well known that fairly serious injuries of the eye may result from puncture wounds or lacerations, but the quantity involved in the mere writing on food products is insignificant and negligible. This is equally true of other constituents mentioned, regardless of their properties under other circumstances and in grossly larger quantities. It is well known that the governmental stamp of inspection on meats is done with methyl violet ink and this imprint is not necessarily removed prior to cooking. It is probable that this dye is otherwise used on food products under governmental sponsorship. While no harm is anticipated, this dye is not included in the list of coal tar dyes which are regarded as harmless and suitable for use in foods, drugs and cosmetics after certification as required by the Food, Drug and Cosmetic Act.

PROBABLE RAGWEED DERMATITIS

To the Editor:—**A man aged 39 has had weeping dermatitis resembling eczema over his face and eyelids for eighteen years. This condition makes its appearance in early August and clears up with the first frost in the fall. He has some lacrimation and stuffiness in his nose. One summer and fall he was in the state of Washington and had complete relief from it. He does not have this condition in Canada either. He is a salesman on the road and works the southern half of Minnesota. I gave him a complete cutaneous testing routine, using Bartos intradermal tests for foods and epidermals, and also tested him with the powdered pollen extracts put up by R. V. Ellis of the University of Minnesota for hay fever (scratch tests). I also tested him for the ten common spores put up by the Abbott Laboratories (skin tests). Of all these he reacted only slightly (1 plus) to house dust and clam. He is anxious to find the offending substance. What further could you suggest in testing or treatment of this skin condition? In the other months of the year the patient's face is clear, and the eruption occurs only on the face and eyelids when it does appear.**

D. E. W. Ellis, M.D., Elgin, Minn.

ANSWER.—This appears to be a plain case of ragweed dermatitis caused by pollen rather than by exposure to the plant itself. Evidence of this conclusion is the date of onset and termination of symptoms, also the fact that symptoms were absent in areas where ragweeds are absent.

None of the tests mentioned could be expected to give positive reactions because the affliction is caused by the oily (lipoid) fraction of the pollen rather than the water soluble portion, which causes whealing of the skin and symptoms of inhalant allergy. If lacrimation and stuffiness of the nose are synchronous with the dermal symptoms, the association would seem to be purely accidental. Successful diagnosis can be carried out only by twenty-four hour patch tests with ragweed oil (obtained by alcoholic or ether extraction of ragweed leaves or ragweed pollen).

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POSSIBLE ACHRESTIC ANEMIA

To the Editor:—**A woman with anemia that does not yield to iron by mouth, to liver or iron injections or to rest and diet has been subjected to an exploration of the abdomen. Every abdominal organ was found to be normal. All tests were negative, including the Wassermann. The blood picture is that of pernicious anemia, but there is acid in the stomach. From my reading in the journals I would call this an achrestic anemia. May I ask the cause, treatment and prognosis? I would appreciate a reply, because the woman's blood is dropping rapidly, her hemoglobin is 42, and the red cells number 2,150,000.**

Mary L. Rosenstiel, M.D., Freeport, Ill.

ANSWER.—The "color index" is about 1 in this patient, so that the anemia is primarily not of the iron deficiency type. If the red blood cells have an average diameter of 7.5 microns, one should consider aplastic anemia or the anemia associated with chronic kidney disease. If the red blood cells are larger than normal, cirrhosis of the liver or myxedema must be considered, although the former would no doubt have been noted at the operation. It is evidently not pernicious anemia. In true plastic anemia the bone marrow, obtained by sternal puncture, would show but little cell growth. In chronic kidney disease the marrow would show active growth of the leukocytes but decreased growth of the red blood cells. In achrestic anemia the marrow would be hyperplastic. For treatment, blood transfusion appears to be indicated. The prognosis depends on the cause, and it is more hopeful if this can be corrected.

SOLIDIFIED CARBON DIOXIDE FOR CARCINOMA OF SKIN

To the Editor:—1. I should like to ask whether carbon dioxide ice or snow is considered good therapy and if it actually destroys basal cell malignant growths if the lesion is small; i. e., by a freezing cauterization of the lesion. Are there any reports of such permanent cures of actual basal malignant growths as proved by biopsy? I have seen it used by others with apparent good results. I have used it myself, apparently successfully, on small cutaneous horns and types of benign epitheliomas. I might ask parenthetically whether it has ever been used successfully on small epidermoids. What could be considered medical uses of carbon dioxide snow or ice? 2. Would you discuss the best therapy for Bowen's disease.

M. C. Hanson, M.D., Loveland, Colo.

ANSWER.—1. Solidified carbon dioxide may be used in some types of small superficial basal cell epitheliomas, though it is not recommended for such use. It is much more effective for removing the keratosis which often precedes the formation of cutaneous horns and some epitheliomas. Other uses for solidified carbon dioxide include the treatment of hemangiomas, some kinds of hairy and pigmented nevi and some telangiectases.

2. Bowen's disease is an intraepidermal carcinoma. It should be treated as a definite form of malignant growth of the skin. Each dermatologist favors some method; each method properly used and chosen for the peculiar circumstance gives comparable results. In each method the entire growth should be removed. It does not make a great deal of difference in the end whether the method is surgical, radiologic or combinations, provided the entire growth is removed. Of course, certain methods are more suitable in one circumstance or another and this is a matter of judgment in each case.

CONSTRICTION IN THE FIELDS OF VISION FOLLOWING NEOARSPHENAMINE THERAPY

To the Editor:—In routine work on the perimeter with patients who have syphilis and are taking neoarsphenamine I find that the field becomes very narrow. Will you tell me where I can get data showing this to be true and the treatment to restore the field to normality? The patients have no papillitis, the arteries and veins are normal, the retina is normal, the macula and fovea are well seen, the media are perfectly clear and there are no corneal opacities; in fact, the fundus is normal in every respect. The patients had a normal field before the arsenic treatment.

R. Marshall Faver, M.D., Miami, Fla.

ANSWER.—It is not the usual thing to find constriction in the fields following the use of neoarsphenamine by patients who originally had normal fields and vision before treatment was started. Unless the patient is susceptible to arsenic or there is already an optic atrophy present, neoarsphenamine should have no effect on the eye or the visual fields. The conditions described are apparently normal though the color of the disks is not mentioned. It may be that there was a beginning optic atrophy.

We know of no publication concerning peripheral fields before and after neoarsphenamine in normal eyes. Any limitation of fields is a definite contraindication to the use of any pentavalent arsenicals, and some authorities say any arsenicals. These patients are usually given malaria or other form of fever therapy. Certainly the drug should be stopped immediately if there should be any constriction of the field of vision, as this is a definite indication of neurosyphilis involving the optic nerve. Fever therapy should be resorted to under these circumstances.

LOSS OF WEIGHT AND OCCUPATION

To the Editor:—A white man aged 40 complains of a loss of weight of 14 pounds (6.4 Kg.) in the past six weeks. Six weeks ago he began to work in a chemical laboratory with crystal urea, formaldehyde, rayon cellulose acetate and various dyes, of which some are vegetable and some are aniline. These chemicals are processed so that the resulting product is a fine powder. He is exposed to this powder at frequent intervals. His appetite has not been affected and his mode of living has not changed. Can the loss of weight be associated with the exposure to these chemicals? Physical examination is essentially negative.

M.D., New Jersey.

ANSWER.—Any reply to this query must be accepted as speculative. In any active laboratory the number of potential exposures always is greater than shown in a casual list such as is here furnished. Loss of weight is associated with many occupational diseases as from dinitrophenol or carbon bisulfide. Urea in large doses (4 Gm. three times a day) will induce weight loss through dehydration, but this degree of intake in a laboratory may not be expected. The diagnostic dictum "Always doubt the significance of a single manifestation" applies particularly to occupational diseases, including the present instance. Loss of weight from industrial substances ordinarily will not arise as the exclusive feature of injury. If dinitrophenol, common to many laboratories that process dyes, might be assumed to be the cause of weight loss, damage to the liver and nervous system or evidences of other injury will coincide with diminution of weight. If loss of weight is other than from apprehension over a new job or from hard work at a new job, full examinations should be made as to possible incipient psychosis, toxic goiter, neoplasm or infectious processes. So far, from the information at hand there is no basis for any linkage with occupation.

RESUSPENDED ERYTHROCYTES FOR TRANSFUSION

To the Editor:—In Red Cross blood banks red blood cells remain after the plasma has been removed from the whole blood by centrifugalizing. If the latter should be diluted with isotonic solution of sodium chloride could this mixture be used for transfusion purposes in cases in which there is a definite indication for red blood cells? Would it be of any value?

Colman Lopatin, M.D., New Haven, Conn.

ANSWER.—Erythrocytes separated by centrifugation of whole blood for the preparation of plasma can be used for transfusions, for example, in anemia, provided certain precautions are taken. First of all, the cells must be used not too long after the blood is drawn, since after storage for a week or longer in citrate solution the survival time of the transfused erythrocytes in the patient's circulation is considerably reduced. Second, the blood samples must be centrifuged individually, because pooling bloods of different groups, as is done by some workers, for example J. M. Hill and E. E. Muirhead, in order to absorb out the isoagglutinins, renders the red blood cells unsuitable for use. Finally, when the erythrocytes and plasma are separated, care must be taken that the centrifugation is not carried out at too high a speed or for too long a time, since excessive packing of the cells damages them and renders them unsuitable for transfusion.

HEMOGLOBIN PREPARATIONS

To the Editor:—I would appreciate references to confirm my opinion that hemoglobin preparations are of little or no value in the treatment of anemias.

M.D., Mexico City, Mexico.

ANSWER.—Truly "organic iron," combined with heme, is not available for hemoglobin production, as it is not released by peptic or tryptic digestion (Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 2, Baltimore, William Wood & Co., 1939, p. 94). Organic iron containing compounds of the type of hemoglobin are without pharmacodynnamic effect (Starkenstein, E.: Die derzeitigen pharmakologischen Grundlagen einer rationallen Eisentherapie, *Klin. Wchnschr.* **7**:217 [Jan. 29] 267, [Feb. 5] 1928). After the ingestion of hemoglobin, the iron containing constituents can be recovered quantitatively in the stools (Haurowitz, F.: Der Abbau des Blutfarbstoffes im Verdauungstrakt des gesunden Menschen, *Arch. f. Verdauungskr.* **50**:33 [Aug.] 1931).

SENSITIVITY TO DUST AND VACUUM CLEANERS

To the Editor:—In the issue of May 23, 1942, in answer to the query concerning vacuum cleaners for dust sensitive people, permit me to call to your attention the fact that the cleaner named "Rexair" permits little or no dust dispersion, as the air intake is passed through a small tank of water. We have one in my own home, and no matter how frequently it is used and fresh water put in each time, the water is a thick mud after each using. I do not know whether this machine is still being produced or on the market, but I assure you that for persons sensitive to dust it is most useful.

Frederick A. Stenbuck, M.D., Mount Vernon, N. Y.

To the Editor:—Regarding the query in Queries and Minor Notes, May 23, entitled "Sensitivity To Dust and Vacuum Cleaners," by a New York M.D., I would suggest the "Rexair" cleaner, made by Rexair, Inc., 1028 Fisher Building, Detroit. The machine contains water in its base and all dust is collected in it, the machine doing several duties, cleaning and conditioning at the same time. It draws all dust particles from the air in the vicinity of the cleaner. Pine oil can also be added to the water container to give a pleasant pine odor to the rooms being cleaned.

Frederick William Meng, M.D., Philadelphia.

ABORTING A COLD

To the Editor:—Referring to the query published in The Journal, April 25, concerning the aborting of a cold, I would state that according to my own experience, which I repeatedly had a chance to corroborate in self experiment during last year, an incipient coryza can be aborted by using iodoform powder as a snuff.

Leo I. Hallay, M.D., Fort Blackmore, Va.